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SOME BIOPHYSICAL PROBLEMS OF VIRUSES*

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Biophysical methods have done much towards obtaining purified viruses and getting from them information useful for the control of disease. The following discussion is not a review[1] of this information but rather a statement of some of the problems which must be met as further progress is made. These problems are threefold, dealing (a) with the concentration, purification and physicochemical properties of viruses, (b) with similar studies of the specific anti-substances that are an animal's response to infection, and (c) with the deeper investigation of virus-antibody interaction that purification makes possible. Their answers are bound to indicate better ways of recognizing viruses and to help in the treatment of disease with antisera and in its prevention with vaccines.

* Work supported in part by a grant from the National Foundation for Infantile Paralysis, Inc.

[1] Literature references to all but current papers can be found in any one of a number of reviews (see, for example, Lennette, Science, 98: 415, 1943) and will therefore not be repeated here.

Because of the size of their particles, purified viral suspensions must have the physicochemical properties associated with colloids. The methods of colloid chemistry were developed to study particles with sizes ranging downwards from about the lower limit of microscopic vision to the larger chemical molecules. For years it was presumed that the particles in all colloidal suspensions were heterogeneous aggregates of smaller particles or molecules, the prevailing sizes being determined more by physical conditions of formation than by ultimate chemical composition. Often this is true, as with inorganic sols, many polysaccharides and the polymers that are the basis of our new plastics, textile fibers and the like: their particles vary, often widely, about some mean value. But Svedberg's demonstration that the particles of many pure proteins are molecules as alike as other molecules in size and shape brought to light an entirely different type of colloid.[2] Some proteins have molecular

weights as low as a few thousands (such as the protamines), others as great as a few millions (for instance, the erythrocruorins). The thousandfold range in weight among them is as great as that between the simplest and the most complex of all other chemical compounds. Viruses extend this range of more or less homogeneous macromolecules or particles another thousandfold before they reach their largest representatives near the lower limit of ordinary microscopic vision. For much of this region they are the only examples yet known of equi-sized particles. But this is probably more because of the attention they have drawn to themselves as producers of disease than because they alone in nature have homogeneous particles of this size. In fact, such non-pathogenic substances are now being encountered through application of the biophysical methods developed to purify viruses. Many more will probably become known as the search for them is expanded.

The biophysical problems of viruses take precedence over those of antibodies and virus-antibody mixtures because purified virus is essential to a serious study of these other questions. The principal things we wish to know now about viruses are, first, how to obtain them pure and in quantities sufficient for the study of their fundamental properties; secondly, the nature, chemical composition, the sizes, shapes and electrical characteristics of their elementary particles, their absorption spectra and the changes produced in them by various forms of radiation and by mild chemicals, and lastly their relation to other macromolecular substances in living cells.

It is obvious that the problem of getting purified virus underlies all others and that the knowledge we can accumulate will be more or less proportional to the amount of purified material available for study. Two things have contributed to make the purification of viruses especially difficult. One has been the chemical instability of most, and the other has been the minute amounts present in many infected tissues. With a few notable exceptions this instability has prevented their successful manipulation by the chemical methods developed for the purification of proteins: it is this which has brought to the fore the gentler physical methods like ultracentrifugation. Most successful purifications have been made from tissues unusually rich in virus. The yields in these cases have with a very few exceptions ranged downwards from about one part by weight per thousand of original tissue to less than a part in a million. From this it is evident that few of the known viruses can now be obtained even in the milligram amounts needed for preliminary studies with purified material. Most studies, especially those of an exploratory character, must therefore be concerned with these few without regard to whether or not they are the most desirable objects from a medical standpoint. Tobacco mosaic, for instance, will continue to command especial interest simply because it can be prepared so easily and cheaply and in such exceptionally large amounts. The quantity of purified virus needed for infection—what might be termed the absolute infectiousness—varies greatly, depending on both the virus itself and its route of invasion; for this reason the percentage of virus in an infected tissue can not be predicted before purification. When infectiousness is high only a few particles weighing perhaps not more than *ca* 10^{-14} gram are needed to produce disease; with other viruses the average infectious dose may be many millions of times greater.

Chemical methods of purification have been applied to crude virus suspensions. The most familiar of these, involving fractional salting-out in strong sulfate solutions, has often been tried. Several plant viruses, including the original preparation of tobacco mosaic, were purified in this way but not without some alteration taking place. Human[3] and mouse[4] poliomyelitis viruses have been concentrated with ammonium sulfate; but here too there is reason to believe that the treatment does not leave the virus unchanged. Selective adsorption and subsequent elution is probably less drastic in its effects on viruses than the foregoing. Large amounts of infectious material can be handled and the potentialities of the method probably have not yet been fully exploited. It was shown years ago that the virus of human poliomyelitis[5] could be partially purified by adsorption on alumina. Specific adsorption of the influenza viruses on red cells[6] has provided an especially simple way of getting large amounts of virus freed from much of the accompanying extraneous material.

A variety of physical procedures has been employed in purifying viruses. Differential ultrafiltration has been used to sort out the virus particles from a suspension of infectious tissue, but the losses are ordinarily too great and the amount of infectious material that can be handled too small to make it a practical method for preparing chemically useful amounts. Partial purifications have also been made by cataphoresis and in a number of other ways, but the methods based on high-speed centrifugation have turned out to be far more useful than others yet proposed. Not long after the initial chemical isolation of the tobacco

[2] Svedberg and Pedersen, "The Ultracentrifuge" (Oxford, 1940).

[3] Clark, Schindler and Roberts, *Jour. Bact.*, 20: 213, 1930; Clark, Rasmusson and White, *Jour. Bact.*, 42: 63, 1941.

[4] Gard and Pedersen, Science, 94: 493, 1941.

[5] Sabin, *Jour. Exp. Med.*, 56: 307, 1932; Schaeffer and Brebner, *Arch. Path.*, 15: 221, 1933.

[6] McClelland and Hare, *Canadian Publ. Health Jour.*, 32: 530, 1941; G. K. Hirst, *Jour. Exp. Med.*, 76: 195, 1942.

mosaic virus it was shown that purified virus could be obtained in large amounts and with less alteration by differential ultracentrifugation; a number of plant and animal viruses have since been purified in this fashion. Present-day ultracentrifuges hold up to 200 cc and develop fields as high as *ca* 200,000 times gravity; machines of larger capacities could be built. They will sediment particles or molecules weighing less than a million and will concentrate lighter molecules with weights down to about 20,000. They can therefore easily handle all known viruses.

Determination of the degree of purity of a refined virus preparation has proved a most difficult problem. Infectivity titrations are useful in the early stages of purification, but they are rarely accurate measures of purity. The analytical ultracentrifuge will show whether the particles in a suspension sediment with the single sharp boundary to be expected if they are alike in size and whether a partially purified preparation still contains either large colloidal or small unsedimentable material. Accurately determined rates of sedimentation also characterize a virus once it has been sufficiently purified. There are, however, several important limitations to observations with the analytical ultracentrifuge as criteria of purity. Under the most favorable conditions less than several per cents of an impurity can not be detected; under other circumstances much larger quantities of undesirable material can be missed. For asymmetric particles such as those of tobacco mosaic, rate of sedimentation is a very poor index of uniformity in particle weight, since in such cases there can be wide differences in particle weight without corresponding differences in sedimentation constant. Sensitivity is further decreased, and the efficiency of the ultracentrifugal method of fractionation can be seriously impaired in viscous tissue suspensions. Though its use for this purpose is only just beginning the electron microscope should ultimately become very helpful in controlling the purity of virus preparations.

One of the first things to be found out about any purified macromolecular substance is the size, shape and degree of uniformity of its constituent particles. Ultrafiltration gives some idea of the particle size of viruses even when applied to impure suspensions, but it can only yield approximate results because ultrafilters do not have uniform pores and filterability depends on other factors besides pore size. The development of the analytical ultracentrifuge for molecular weight determination and the large mass of data accumulated with this instrument are well known. Of the two ways to find weights from centrifugal observations only that utilizing rates of sedimentation is applicable to particles as big as viruses. Besides these rates it is necessary to know other properties both of the purified virus particles—density and shape—and of its suspensions—viscosity, rate of diffusion and degree of hydration. Diffusion can be accurately measured by one of several experimental procedures and a rough estimate of particle shape can be derived from studies of viscosity, of streaming double refraction and from other more or less indirect observations. The density of virus particles can not be measured in a straightforward manner. Perhaps the best available estimates arise from comparisons of rates of sedimentation in media of different known densities, such as strong sugar[7] or albumin[8] solutions. How closely these values approach the densities of native virus particles depends in large measure on how much the particles are altered by the abnormal osmotic environment of such solutions; in this respect determinations in albumin should be superior to those in sugar. An interesting but as yet little-used technique[9] for getting densities involves measurement of sedimentation rates in dilute suspensions made up with ordinary and heavy water. In spite of prevailing inaccuracies ultracentrifugal measurements give data about the weights of virus particles which will become increasingly accurate as time goes on. Rates of sedimentation are best determined with the optical ultracentrifuge, but they can also be estimated from biological or chemical analyses[10] of successive layers in an undisturbed tube after quantity ultracentrifugation. This is not accurate, but it can be used with crude virus suspensions and with solutions too dilute to give the optical effects required in the first procedure.

The electron microscope provides a direct and independent way of estimating the sizes and shapes of viruses. Its greatest uncertainty lies in the sure identification of the particles of virus among the numerous objects of small size that can be seen in an average preparation. This uncertainty will of course diminish as more observations are made on material of greater purity. Probably the greatest inaccuracy in electron microscopic estimates of size lies in the present lack of knowledge of the amount of shrinkage and distortion involved in making the necessary preparations. The ability to see virus particles makes many interesting questions accessible to study. For example it supplies a direct way of determining (a) how closely direct observation agrees with deductions from ultracentrifugation and other indirect measurements, (b) what if anything particle-morphology as seen in purified virus prepa-

[7] Elford and Andrewes, *Brit. Jour. Exp. Path.*, 17: 422, 1936; Smadel, Pickels and Shedlovsky, *Jour. Exp. Med.*, 68: 607, 1938.

[8] Sharp, Taylor, McLean, Beard and Beard, SCIENCE, 100: 151, 1944.

[9] Lepine, Levaditi and Guintini, *Compt. rend.*, 214: 768, 1942.

[10] Elford and Andrewes, *op. cit.;* Pickels, *Jour. Gen. Physiol.*, 26: 341, 1942–3; etc.

rations tells about viruses under actual conditions of growth and multiplication, and (c) how uniform these particles are in size and shape. In a general way ultracentrifuge and electron microscope seem to corroborate one another when observations are made on comparable material. Thus purified preparations of the tobacco mosaic virus[11] exhibit the elongated threads predicted by the ultracentrifuge and its associated methods, while the particles seen in bushy stunt virus are the roundish bodies to be expected from sedimentation data. The pictures of the papilloma virus, however, show more spherically symmetrical objects than have been predicted from other measurements.[12] It has already been stated that the electron microscope should prove helpful in controlling the purity of virus preparations. Such control will come through the study of representative fields taking account of everything present instead, as is often now the custom, of concentrating on atypical fields showing only virus particles. It is reasonable to look to the electron microscope for direct information as to how viruses multiply. For this they must be examined not in purified preparations but as nearly as possible under the conditions in which they are produced, or reproduced, in nature. During the last few years there has been much fruitless discussion as to whether viruses are "alive." This debate has been futile, not because it is inherently meaningless, as is frequently stated, but because there have been no experimental data bearing on the question. Very probably the study and photography of viruses within infected cells could give such data. Two problems are involved in the electron microscopy of sectioned material. Suggestions have been made concerning the design of special microtomes to cut thin enough sections, but they may not be needed at this time since electron microscopic pictures can apparently be made of biological material a micron thick and there are standard microtomes that can cut down to half this thickness. The other and perhaps more difficult problem concerns handling and mounting these very thin sections so that they do not suffer too much distortion during desiccation. There has also been considerable discussion of the importance of devising ways of photographing living material[13] with the electron microscope. This probably would not be as valuable as one might think if only because Brownian movement in living cells is sufficient to blot out all structures so fine that it needs the electron microscope to reveal them.

[11] Stanley and Anderson, *Jour. Biol. Chem.*, 139: 325, 1941; 146: 25, 1942.

[12] Sharp, Taylor, Beard and Beard, *Proc. Soc. Exp. Biol.*, 50: 205, 1942.

[13] von Ardenne, *Naturw.*, 29: 521, 1941; Abrams and McBain, SCIENCE, 100: 273, 1944.

The particles of a virus can not justifiably be considered as very large chemical molecules unless they are uniform in size. None of the larger viruses, such as vaccinia or influenza, has yielded the sharp centrifugal boundaries to be expected from a suspension of uniform particles. Electron microscopy too indicates that the elementary bodies of these big viruses[14] vary considerably about a mean size, though its evidence can not be convincing until more is known about how these particles change on drying. On the other hand, the boundaries from several of the smaller viruses are very sharp. This points to a great uniformity in size when the particles are nearly spherical, as they are with bushy stunt, for example.[15] Very probably such particle-uniformity is one of the essentials for the growth of well-defined crystals. Where elongated particles are involved, as with the tobacco mosaic and long-chain polymers, sharpness of sedimenting boundary is not adequate evidence of uniform particle weight. This too is borne out by electron microscopic observations that show the tobacco mosaic as consisting of particles of various lengths. These viruses give fibrous aggregates rather than well-defined crystals. Knowledge of such incompletely crystalline materials is still fragmentary, but x-ray and electron diffraction is giving more and more information about them. Some of the x-ray diffraction effects from purified tobacco mosaic virus[16] are apparently due to incomplete regularities in particle arrangement and others to repetitions within the particles themselves. Electron diffraction should prove especially valuable in the study of structures of this sort because it requires very small amounts of material and will reveal regularities in films and other thin structures. Thus it becomes feasible, especially when electron microscopy is combined with diffraction to gain a deep insight into the details of many biological structures; the important work now being done on connective tissue[17] shows how much can be learned in this fashion. These techniques may teach much about the internal structure of viruses and even about their interaction with the cells they invade.

Since there is yet no straightforward way to establish the purity of a refined virus preparation it is important to use every indirect method capable of throwing light on the subject. Electrophoresis, by providing accurate rates of migration in an electrical field, is such a method. Except for patterns demonstrating the electrophoretic homogeneity of certain

[14] Green, Anderson and Smadel, *Jour. Exp. Med.*, 75: 651, 1942; Taylor, Sharp, Beard, Beard, Dingle and Feller, *Jour. Immun.*, 47: 261, 1943; 48: 129, 361, 1944.

[15] Lauffer, *Jour. Biol. Chem.*, 143: 99, 1942.

[16] Bernal and Fankuchen, *Jour. Gen. Physiol.*, 25: 111, 147, 1941–2.

[17] Jakus, Hall and Schmitt, *Jour. Am. Chem. Soc.*, 66: 313, 1944; etc.

plant viruses,[18] of the papilloma virus[19] and of vaccinia and its antigens,[20] little work of this sort has been done with purified viruses largely because existing techniques require more material than is ordinarily available. Some dyes combine and migrate with proteins; if they react similarly with purified viruses it may be possible to work with much less virus. It will also be important to determine how much the electrical properties of a virus are influenced by other components of the tissues in which it grows. The elementary bodies of vaccinia migrate at the same rate as its soluble heat-stable antigen. The virus of African horse sickness moves[21] at the speed of albumin and it has been suggested that this may be an index of an association between the two. A complete study of the electrical mobility of a virus gives an accurate knowledge of its isoelectric point. Many determinations of isoelectric point have been made on crude suspensions of virus-diseased tissues. Such results, however, can be very misleading because the isoelectric points of tissue proteins may be different from that of virus and the predominance of these proteins may thoroughly mask what is happening to the virus.

The fundamental question of chemical composition can be approached only with considerable amounts of fully purified virus. It is therefore inevitable that the chemical work now possible will center around a few viruses, like the plentiful plant viruses, influenza, vaccinia, the equine encephalomyelitises, the rabbit papilloma and mouse poliomyelitis. A satisfactory knowledge of virus composition will probably be reached only by a process of successive approximations since much analytical work will inevitably be done on material found later to be impure. Hence for some time to come all information about composition will be provisional. Probably all viruses are nucleoproteins. The small viruses appear to be only nucleoprotein, but if vaccinia[22] is typical the larger viruses contain fat, carbohydrate and many other constituents common to microorganisms. Influenza[23] has seemed similarly complex, but this can not be considered as proved since recent work[24] has demonstrated non-viral substances of like composition in refined virus and in the fluid of undiseased embryos. Unusual amounts of copper have been found in purified vaccinia. It will be interesting to find out whether small as well as large viruses show a concentration of metal and whether it is always copper. One of the most desirable things to know would be the amino-acid content of virus protein. This analysis by classical methods is so difficult and consumes so much material that there is no hope of getting enough of any virus except the tobacco mosaic for such a study. The use of heavy isotopes and of bacteria of known amino-acid nutritional requirements is creating new analytical procedures, however, and there are several unexplored physical approaches which if developed may make possible the analysis of viruses. The presence of histidine in the rib-grass but not in other strains of tobacco mosaic[25] suggest that viruses will show significant differences in their amino acids.

Our ideas that the chemical specificity of living tissue is uniquely dependent on its proteins may be drastically modified by the recent demonstration[26] that specific nucleic acids determine the transformation of one type of pneumococcus into another. In these experiments the addition of a definite chemical substance has for the first time altered in predetermined fashion the inheritable properties of a living cell. If this is not an isolated example, then an understanding of the nucleic acids of viruses will be as valuable as a knowledge of their specific proteins. It will be important to determine if the development[27] of transmissible myxomatosis by injecting killed myxoma and living fibroma viruses together into a rabbit is due to the myxoma's nucleic acid. From a chemical standpoint nucleic acids appear simpler than proteins; if they are as numerous as the proteins their differences from one another must reside in the size of their molecules and the structural relationships between the few different nucleotides from which they are built. Nucleic acid preparations have not been crystalline and x-ray diffraction has thus far given little useful information about them. It is now evident that they are at least as easily damaged as proteins; less altered material will be needed for further studies in the ultracentrifuge and by x-ray diffraction. It remains to be seen whether the electron diffraction and microscopic techniques will help.

Viruses have been especially easy to recognize through the diseases they produce, but we are now learning that other substances of similar particle size exist. These substances frequently complicate and even render impossible the purification of viruses. In fortunate instances they are less stable or sufficiently different in size to be separable by a selective procedure such as ultracentrifugation. But cases are be-

18 Lauffer and Ross, *Jour. Am. Chem. Soc.*, 62: 3296, 1940; McFarlane and Kekwick, *Biochem. Jour.*, 32: 1607, 1938; Melchers, *et al.*, *Biol. Zentr.*, 60: 524, 1940.

19 Sharp, Taylor, Beard and Beard, *Jour. Biol. Chem.*, 142: 193, 1942.

20 Shedlovsky and Smadel, *Jour. Exp. Med.*, 72: 511, 1940; Smadel, Pickels, Shedlovsky and Rivers, *ibid.*, 72: 523, 1940.

21 Polson, *Onderstepoort J. Vet. Sci.*, 16: 51, 1941.

22 Hoagland, *et al.*, *Jour. Exp. Med.*, 71: 737; 72: 139, 1940; 74: 69, 133, 1941; 76: 163, 1942.

23 Taylor, Sharp, McLean, Beard, Beard, Dingle and Feller, *Jour. Immun.*, 48: 361, 1944.

24 Knight, *Jour. Exp. Med.*, 80: 83, 1944.

25 Knight, *Jour. Am. Chem. Soc.*, 64: 2734, 1942.

26 Avery, MacLeod and McCarty, *Jour. Exp. Med.*, 79: 137, 1944.

27 Berry, *Arch. Path.*, 24: 533, 1937.

ing found where viruses have much the same size and stability as components of the healthy tissues involved. Mouse lungs infected with influenza[28] provide an example. Ultrafiltration or centrifugation of normal lungs yields a suspension of particles about 100 mμ in diameter. Infectiousness is found associated with particles of this size when infected lungs are similarly treated, and it has required much work to prove that the virus itself is not a far smaller entity adsorbed to "healthy" 100 mμ particles. Allantoic fluid from infected embryos is an especially valuable starting point for the preparation of purified influenza virus, but even with this favorable material the end product is often not more than 50 per cent. virus. A similar situation has been described[29] from the study of infectious jaundice, or grasserie, of silkworms. In a recent ultracentrifugal investigation it was shown that the virus activity was sedimented at the rate of 17×10^{-13} s units; but there are macromolecules in healthy silkworms which sediment at the same rate, 16×10^{-13} s. The non-infectious macromolecules just referred to are not isolated instances of such substances. No survey has yet been made to determine how widespread they are in living tissues and we know only about those that have been encountered by accident. Many healthy plants contain macro-substances of moderate stability and complexes have been isolated which are unstable chlorophyll-protein compounds.[30] Macromolecular substances have been prepared from the tissues as well as from the allantoic fluid of healthy chicken embryos. Materials of the same order of size can be extracted from brain, spleen and from a wide variety of other tissues. It has been shown that macromolecules from lung[31] are carriers of strong thromboplastic activity. With this exception little is known of the functions of these macromolecules and whether they are primary constituents of cells or products of cell disintegration. It has been suggested that what was isolated from chicken embryos were either mitochondriae or threads of chromatin from cell nuclei. Evidently much more work will be required before there is a real understanding of these "normal" substances.

A knowledge of the mechanism of virus inactivation has become especially important with the proof that killed virus vaccines give effective protection against infection. This mechanism can only be studied with the help of pure viruses. Practical vaccine production also is increasingly concerned with purified viruses because, everything else being equal, vaccines made from them will be superior to those made with crude tissue suspensions. As yet there is little understanding of the changes that take place in a virus particle during inactivation either by chemicals or radiation. Effective killed virus vaccines are made with formaldehyde, but the reaction is in fact unknown and we are in no position to say whether the essentially empirical procedures now employed in making vaccines are the most desirable ones. A knowledge of the absorption spectrum of purified viruses provides a similar sound basis for investigations into the best way to produce vaccines through photo-inactivation. The absorption spectrum of a pure protein sometimes gives limited information about its composition. Of the few purified viruses thus far examined[32] all but the yellow fever virus have the not especially characteristic spectrum of a nucleoprotein with intense absorption around 2,600A and rather complete transmission everywhere else in the near ultraviolet and visible regions. For the yellow fever virus, however, extraordinarily intense absorption has been reported[33] from about 3,200A to the visible. The reason for this is not known, but the virus must either contain an intense chromophoric component or be associated through chemical combination or otherwise with some intensely absorbing tissue or serum protein. If this yellow fever absorption is diagnostic for virus it permits a purely physical assay of the minute amounts that are biologically significant.

Many of the problems of viral antibodies are the same as those already discussed in connection with the viruses. Compared with what is known about other antisera our knowledge of sera against viruses is very scanty. This is largely due to the relative weakness of most such sera, as shown for instance by electrophoretic analysis, and to the difficulty of making quantitative measurements of reactions between these poor sera and crude virus suspensions. Purified viral antibodies are therefore needed for fundamental biophysical work; to get them involves both the production of more potent sera and the concentration and purification of the antibodies thus produced. Sera of the highest antibody content are only obtained after often-repeated injections of large amounts of immunizing antigen. Since there is little virus by weight in most infectious tissues it is not surprising that hyperimmune sera made with them contain little viral antibody even when their neutralizing titres seem high. Their electrophoretic patterns show this clearly. It has been repeatedly demonstrated that hyperimmunization with bacteria, toxin or a purified protein enhances the small gamma-peak of a normal animal serum or introduces a new peak nearby which in-

[28] Chambers and Henle, *Jour. Bact.*, 42: 434, 1941; *Am. Jour. Path.*, 17: 442, 1941; *Jour. Exp. Med.*, 77: 3, 1943; Stanley, *Jour. Exp. Med.*, 79: 267, 1944.

[29] Glaser and Stanley, *Jour. Exp. Med.*, 77: 451, 1943.

[30] Smith and Pickels, *Jour. Gen. Physiol.*, 24: 753, 1940–1; Fishman and Moyer, *ibid.*, 25: 755, 1941–2; etc.

[31] Chargaff, Moore and Bendich, *Jour. Biol. Chem.*, 145: 593, 1942.

[32] Taylor, Sharp, Beard, Finkelstein and Beard, *Jour. Inf. Dis.*, 69: 224, 1941; etc.

[33] Pickels and Bauer, *Jour. Exp. Med.*, 71: 703, 1940.

creases with continued hyperimmunization till it predominates over all other features of the pattern. No antiviral serum has yet shown this, and few[34] that have been examined have contained enough antibody to provide a detectable electrophoretic peak, new or enhanced. It may be that hyperimmune sera will never be of value in the treatment of most viral infections, but before drawing such a conclusion at this time it is well to remember how hard it would be to prove the undisputable curative qualities of antipneumococcal or antidiphtheretic sera using preparations containing no more antibody than do present-day antiviral sera. Good hyperimmune sera against many viruses probably can not be produced in any considerable amounts until future discovery provides richer sources of virus-antigen; nevertheless, progress can now be made by working with purified viruses and by developing immunizing schedules with adjuvants that will best utilize what virus is available.

More potent antiviral sera will in themselves be purer, but it should be possible to purify them further by the kind of chemical fractionation applied to other sera. Some viral antibodies, such as those against hog cholera or the measles antibody in human blood, are concentrated by salting-out, but it is commonly supposed that others, such as some sera against encephalomyelitis, are easily destroyed by these procedures. Very little can be said about the chemical fractionation of viral antibodies until much more careful work has been carried out. In a few trials viral antibodies have not shown the pronounced resistance to peptic digestion that characterizes antitoxins and makes their purification so easy; the possibilities of using milder methods of digestion under carefully controlled conditions should be thoroughly explored.

Purified virus and antibody permit a completely new approach to problems of virus-antibody interaction. More knowledge of this interaction is needed for gauging the prophylactic and therapeutic possibilities of viral sera; it is equally essential to any serious attempt to develop and refine the various methods of virus and antibody detection based on it. There has been prolonged discussion as to whether the product of virus-antibody interaction is fundamentally different from bacterial-antibody and from other antigen-antibody combinations. The root of this debate lies in observations[35] that certain non-infectious virus-antibody mixtures become sources of disease when sufficiently diluted. This apparent recovery of free virus has been taken to prove that the virus-antibody complex dissociates readily. It is of the greatest importance to know whether this is correct because it would set an obvious limit to the sensitivity that could be attained by any diagnostic method based on the virus-antibody interaction. All that can be said at present is that, while dissociation may occur, there are other plausible explanations[36] of the dilution phenomenon, and crucial experiments have not yet been made. In any event the most direct way to increase the sensitivity of virus and antibody detection lies in finding out how to recognize minimal amounts of virus-antibody interaction. Complement-fixation is based on interactions involving virus or the associated soluble antigens, and great progress[37] has lately been made in identifying virus infections by using purer antigens and more carefully controlled conditions of test; it is not known whether the technical difficulties in converting it into a micro-method can be met. Several other ways of recognizing traces of virus-antibody suggest themselves. One of these would take advantage of our ability to see single virus particles under the electron microscope. To the degree that there is a firm union between virus and antibody it is reasonable to seek evidence for this in some alteration in the appearance of elementary virus particles or in their association together. This seems to occur when antibody is added to the tobacco mosaic virus.[38] An increase in sensitivity of virus and antibody detection may also be possible through the use of foreign particles coated with virus. As is well known, such particles, of silica or collodion, for example, may cover their surfaces with an adsorbed protein and thereby take on many of its physicochemical properties.[39] There have been several claims[40] of successful precipitation tests diagnostic for viruses performed with bacteria and with collodion particles acting as adsorbents, though careful studies[41] have failed to confirm these results. Foreign particles will behave as viruses only if their surfaces are completely virus-coated and it would seem hard to achieve this condition with crude virus or by adsorption on bacteria whose surfaces must be complex records of the varied conditions of their growth. Experiments of this type should therefore be repeated with purified virus and with collodion or other particles prepared under carefully controlled conditions. Microelectrophoretic examination of virus-coated par-

[34] Sharp, Taylor, Beard and Beard, *Proc. Soc. Exp. Biol.*, 50: 358, 1942.

[35] Sabin, *Brit. Jour. Exp. Path.*, 16: 70, 84, 158, 169, 1935; Beard, Taylor, Sharp and Beard, *Jour. Inf. Dis.*, 69: 173, 1941; etc.

[36] Morris, *Jour. Immun.*, 48: 17, 1944; Hershey, Kalmanson and Bronfenbrenner, *ibid.*, 48: 221, 1944; etc.

[37] Casals and Palacios, Jour. Exp. Med., 74: 409, 1941; *Am. Jour. Pub. Health*, 31: 1281, 1941; Havens, Watson, Green, Lavin and Smadel, *Jour. Exp. Med.*, 77: 139, 1943; Casals, SCIENCE, 97: 337, 1943.

[38] Anderson and Stanley, *Jour. Biol. Chem.*, 139: 339; 140: 3, 1941.

[39] Abramson, Moyer and Gorin, "Electrophoresis of Proteins" (New York, 1942).

[40] Goodner, SCIENCE, 94: 241, 1941; Roberts and Jones, *Proc. Soc. Exp. Biol.*, 47: 75, 1941; 49: 52, 1942; Weil, *Jour. Immun.*, 45: 187, 1942; Weil, Popken and Black, *ibid.*, 48: 355, 1944.

[41] Pearson, *Jour. Immun.*, 49: 117, 1944.

ticles[20] may provide another way of detecting traces of antibody, as well as of measuring the electrical properties of purified viruses that can not be obtained in amounts sufficient for the usual electrophoretic procedures. Some antigen-antibody reactions alter the viscosity[42] and the light-scattering of systems in which they occur; it is not yet known if these things happen when the antigen is a virus. Whether the most useful method turns out to be one of the foregoing, or some other, it seems certain that better ways of detecting minimal amounts of antibody will result from the use of purified viruses; and as antibodies are purified they will in the same fashion enhance the sensitivity of virus-detection.

[42] du Noüy, "La Température critique du Sérum" (Hermann et Cie, Paris, 1936), Chap. III.

OBITUARY

FREDERICK SLOCUM

AFTER an illness which had confined him to the college infirmary for about six weeks, Dr. Frederick Slocum, professor of astronomy at Wesleyan University and director of the Van Vleck Observatory, died on December 4 at the age of seventy-one years.

Professor Slocum had three leading interests, scientific research, teaching and the sea; and these three interests seemed to share his energy and his affections without dividing them. His knowledge of sailors, ships and fish enriched his teaching; and sailing and fishing gave him needed relaxation from his administrative and teaching duties.

He was born at Fairhaven, Massachusetts, on February 6, 1873, the son of Frederick and Lydia Ann Jones Slocum. His father was captain of a whaling ship, and Frederick's early years were spent in a nautical environment. During the long summers on Cuttyhunk Island he became skilful in sailing and in navigation and acquired a love of the sea which he never lost, although in later years his profession sometimes required him to live far inland.

In 1891 Mr. Slocum entered Brown University, and for eighteen years as student and teacher he was connected with that institution, receiving the degrees of A.B., A.M. and Ph.D. in 1895, 1896 and 1898, respectively. A fourth Brown degree, the honorary doctorate of science, was conferred upon him in 1938. After receiving the baccalaureate degree, he served as instructor in mathematics for five years and then as assistant professor of astronomy for nine years. During this period he was profoundly influenced by Professor Winslow Upton, by whom he was inspired to make astronomy his life work.

In 1899, while still at Brown, Dr. Slocum married Carrie E. Tripp, who was his constant companion at home and abroad until her death in 1942.

During the years spent at Brown in close association with Professor Upton, Dr. Slocum became an outstanding teacher. He remained a teacher for the rest of his life, but in 1908–09, while on leave from Brown, a year spent as volunteer assistant in the Royal Astrophysical Observatory of Potsdam marked the beginning of a fruitful research career.

After the year in Germany, Dr. Slocum returned to America to join the staff of the Yerkes Observatory of the University of Chicago. Here he worked with the recently invented spectroheliograph, studying the circulation of the solar atmosphere, and he was one of the first to call attention to the fact that matter from solar prominences seemed to move toward and into near-by sunspots. In addition to the solar work Dr. Slocum continued the stellar parallax program started by Schlesinger, introducing the use of Wallace's color filters to produce sharper photographic images.

The years at Yerkes were devoted primarily to research, but Dr. Slocum was still a teacher, and graduate students who came to Williams Bay for the observational part of their training soon learned that in him they could find a skilful guide and a friendly counselor.

In 1914 Dr. Slocum was called to Wesleyan University as professor of astronomy. There his first task was to plan the new Van Vleck Observatory and supervise its construction. In choosing for the principal instrument of the observatory a twenty-inch visual refractor, he had in mind the continuation of his stellar parallax observations and also the requirements of a fairly extensive teaching program. The observatory staff soon increased to four in number, and under Dr. Slocum's leadership a regular program of parallax and other astrometric observations was maintained until the establishment of a Naval Flight Preparatory School at Wesleyan in 1942 made it necessary for the members of the staff to devote all their time to teaching. Although beyond the usual retiring age, Professor Slocum carried his full share of the teaching load until failing health necessitated his retirement on November 1, 1944.

The continuity of Professor Slocum's work at Wesleyan was broken by an absence of three years from 1917 to 1920, when he served for one year as instructor in navigation for the United States Shipping Board and for two years as professor of nautical science at Brown University.

During his year at Potsdam and during several later trips to Europe, Professor Slocum made many friends among the astronomers of other lands, and

he was active in the affairs of the International Astronomical Union from its very beginning. He was a fellow of the Royal Astronomical Society of England and a member of the Astronomische Gesellschaft and of the Société Astronomique de France. At home he had served as vice-president of the American Astronomical Society and as vice-president of Section D of the American Association for the Advancement of Science, and for three years he had been a member of the National Research Council. He was a member of the American Academy of Arts and Sciences. He was a member of Phi Beta Kappa and of Sigma Xi, but his membership in these fraternities did not consist solely in having his name on the list; he was an active participant in the affairs of their Wesleyan chapters.

As a quiet but effective advocate of good-will and cooperation both at home and abroad, as an inspiring teacher and congenial colleague, Professor Slocum will long be remembered by a world-wide circle of friends and acquaintances.

CARL L. STEARNS

RECENT DEATHS

WILLIAM BENJAMIN GREGORY, professor emeritus of experimental engineering and hydraulics of Tulane University, died on January 29. He was in his seventy-fourth year.

DR. EDWARD E. REINKE, professor of biology at Vanderbilt University, chairman of the division of natural science and mathematics, died on January 25. He was fifty-seven years old.

SCIENTIFIC EVENTS

THE UNITED STATES COMMITTEE FOR THE STUDY OF PARICUTIN VOLCANO

LAST June at the annual meeting of the Section of Volcanology of the American Geophysical Union, a symposium on the current activity of the infant Mexican volcano, Paricutin, caused the retiring officers to recommend to the National Research Council that a committee be formed under its auspices to integrate the study of the eruption and its effect before the opportunity was lost. The chairman of the Division of Geology and Geography then invited Richard E. Fuller, the newly elected president of the section, to assume the responsibility of serving as chairman.

By the end of July, the U. S. Committee for the Study of Paricutin Volcano was organized and approved with the stated objective: "The purpose of the committee is to coordinate with Mexican scientists the research on the Paricutin volcano and to encourage and facilitate studies in various scientific fields related to the problem. It intends thereby to avoid useless repetition and especially to save from neglect important aspects which depend on the collection of accurate data before activity subsides and the record of eruption is obscured by time. The scope of the proposed investigation includes geological, geophysical, chemical, meteorological and other scientific studies. The committee would endeavor to stimulate the interest and the support of scientific organizations and governmental agencies in these various projects." The initial members were Richard E. Fuller, *chairman*, research professor of geology, University of Washington; Fred M. Bullard, professor of geology and mineralogy, University of Texas; W. F. Foshag, curator of mineralogy, U. S. National Museum; L. C. Graton, professor of mining geology, Harvard University; D. F. Hewett, special staff scientist, U. S. Geological Survey; A. G. McNish, magnetician, Department of Terrestrial Magnetism, Carnegie Institution; Paul A. Smith, chief, Aeronautic Chart Branch, U. S. Coast and Geodetic Survey; O. W. Swainson, chief, Division of Geomagnetism and Seismology, U. S. Coast and Geodetic Survey; C. Warren Thornthwaite, chief, Climatic and Physiographic Division, Soil Conservation Service, U. S. Department of Agriculture; Howel Williams, professor of geology, University of California; E. G. Zies, chemist, Geophysical Laboratory, Carnegie Institution; William W. Rubey, *ex-officio*, chairman, Division of Geology and Geography, National Research Council. Subsequently, the committee was enlarged to include O. O. Fisher, of Detroit; Robert T. Hatt, director of the Cranbrook Institute of Science, and Ezequiel Ordóñez, chairman of the corresponding Mexican committee, and Vocal Geológo de la Comisión Impulsora y Coordinadora de la Investigación Científica.

Under the sponsorship of the Comisión Impulsora, Ordóñez, who has been principally responsible for recording the activity of the volcano, formed the Comite Mexicano para el Estudio del Volcan de Paricutin, with the following membership: Teodoro Flores, director del Instituto de Geología; Ricardo Monges López, director de la Facultad de Ciencias; Pedro C. Sánchez, director del Instituto Panamericano de Geografía e Historia; Manuel Medina, Jefe del Departamento de Geografía y Meteorología de la Secretaria de Agricultura; Alfonso de la O Carreño, Jefe del Departamento de Geología de la Comisión Nacional de Irrigación; Hermión Larios, Departamento de Exploraciones de Petróleos Mexicanos;

Ramiro Robles Ramos, Geológo de la Comisión Nacional de Irrigación. This committee has recently been allotted a substantial fund by the Mexican Government.

The support of the State Department's Interdepartmental Committee for the Cooperation with Latin American Republics has made possible two of the major projects which were submitted by the U. S. Geological Survey and the U. S. Coast and Geodetic Survey. The Geological Survey has assigned Howel Williams to map the region with the assistance of Kenneth Segerstrom as topographer, and thus to supplement the record of Ordóñez, Foshag and others, while the Coast and Geodetic Survey is having seismic and magnetic observations made by their volcanological geophysicist, Austin E. Jones, who will have as a background the recently published report of the preliminary studies made by that governmental agency during 1943.

The Geological Society of America has generously allotted a grant from The Penrose Fund to Fuller, as chairman, for the accession, construction and maintenance of shelters, trails and other physical facilities at the volcano, and has very substantially earmarked additional funds for other projects that may be recommended by the Paricutin Committee and approved by the project and executive committees of the society. The physical improvements have been made increasingly necessary owing to the difficulties imposed by the continued activity of the volcano, which in recent months has erupted extensive flows in various directions. They are also required for the installation of instruments in a region where throughout the year one usually contends with either rain or dust, and, incidentally, with the depredations of tourists.

Through the cooperation of the Carnegie Institution, E. G. Zies, volcanological chemist of the Geophysical Laboratory, visited Paricutin during November and December in order to become better equipped to serve the committee as counselor and adviser. He was also helpful in defining feasible and potentially diagnostic geophysical projects. Although some of these phases of investigation have to be carried on during the course of the eruption, others can only be successfully pursued after the activity has largely subsided. The committee is also sponsoring studies of related biological problems in the hope of correlating all critical data concerning the eruption.

NOMINATION OF OFFICERS OF THE AMERICAN INSTITUTE OF ELECTRICAL ENGINEERS

THE National Nominating Committee of the American Institute of Electrical Engineers, consisting of members from various parts of the country, has nominated the following official ticket of candidates for the offices becoming vacant on August 1, 1945:

For President: W. E. Wickenden, president, Case School of Applied Science, Cleveland, Ohio.

For Vice-Presidents (Middle Eastern District): Ernest S. Fields, vice-president, Cincinnati Gas and Electric Co. (Southern District): Herman B. Wolf, superintendent of maintenance, Duke Power Co., Charlotte. (North Central District): L. M. Robertson, transmission and station engineer, Public Service Co. of Colorado, Denver. (Pacific District): F. F. Evenson, consulting engineer, San Diego. (Canada District): F. L. Lawton, assistant chief engineer, Aluminum Company of Canada, Montreal.

For Directors: John M. Flanigen, distribution engineer, Plant Accounting, Georgia Power Co., Atlanta. J. R. North, assistant electrical engineer, Commonwealth and Southern Corporation, Jackson, Mich. W. C. Smith, Pacific district engineer, General Electric Co., San Francisco.

For National Treasurer: W. I. Slichter, professor emeritus of electrical engineering, Columbia University.

These official candidates, together with any independent nominees that may be proposed later in the manner specified by the Constitution and By-laws, will be voted upon by the membership at the coming election this spring.

AWARDS OF THE INSTITUTE OF THE AERONAUTICAL SCIENCES

A MEETING of the Institute of the Aeronautical Sciences was recently held in The Engineering Societies Building, New York City, under the presidency of R. H. Fleet.

Honorary fellowships were awarded to Dr. Edward P. Warner, vice-chairman of the Civil Aeronautics Board, and to Sir Frederick Handley Page. Colonel Sir Vivian Gabriel, of the British Air Commission to Washington, accepted for Sir Frederick.

Fred E. Weick, chief engineer of the Engineering and Research Company of Riverdale, Md., received the Sylvanus Albert Reed Award for a contribution to aeronautical science in recognition of his development of the two-control, non-spinnable Ercoups in the small plane field.

The John Jeffries Award for contributions to aeronautical medicine went to Air Marshal Sir Harold E. Wittingham, director general of medical sciences of the Royal Air Force.

The Octave Chanute Award was conferred on Colonel Benjamin S. Kelsey, of the Army Air Forces, for his work in testing high-speed aircraft.

The Robert M. Losey award was conferred on John Cary Bellamy, special consultant to the Weather Service of the Air Forces, who is now in the Pacific, for his contributions to meteorology during the year. The award was accepted for Mr. Bellamy by Dr. Horace R. Byers, of the University of Chicago.

The Lawrence Sperry Award for the best contributions of a young man to aeronautical science was given

to William H. Phillips, head of the stability and control flight section at Langley Field.

A number of fellowships and honorary memberships in the institute were conferred.

AWARD OF THE GOLD MEDAL OF THE AMERICAN INSTITUTE OF CHEMISTS

The gold medal of the American Institute of Chemists, presented annually for "noteworthy and outstanding service to the science of chemistry or the profession of chemist in America," was awarded on February 2 to John W. Thomas, chairman and director of the Firestone Tire and Rubber Company. The medal was given in recognition of his leadership in rubber research for four decades and for achievements under his direction in the development and production of synthetic rubber.

Former recipients of the medal include Dr. Willard H. Dow, president of the Dow Chemical Company; Andrew W. Mellon, the late Secretary of the Treasury, and his brother, the late Richard B. Mellon, of Pittsburgh; James Bryant Conant, president of Harvard University, and the late George Eastman, founder of the Eastman Kodak Company.

Formal presentation of the medal will be made on May 11 at Columbus, Ohio, during the twenty-third annual meeting of the institute. The chairman of the committee arranging the conference is E. L. Luáces, president of the Chemical Developments Corporation, Dayton, Ohio, and chairman of the Miami Valley Chapter of the institute. Dr. James R. Withrow, head of the department of chemical engineering of the Ohio State University, is honorary chairman.

During the last year, Mr. Thomas has supervised the designing and construction of a $2,000,000 rubber research laboratory which is one of the most modern and complete in the world. This laboratory will be dedicated within the next few months.

The jury of chemists making the award was composed of Dr. Gustav Egloff, petroleum technologist of the Universal Oil Products Company; Dr. Harry L. Fisher, director of research for U. S. Industrial Chemicals, Inc.; Dr. Robert J. Moore, manager of the Development Laboratory of the Bakelite Corporation; Dr. Maximilian Toch, president of Toch Brothers, Inc., and chairman of Standard Varnish Works, and Howard S. Neiman, secretary of the institute.

SCIENTIFIC NOTES AND NEWS

Dr. Thomas M. Rivers, director of the Hospital of the Rockefeller Institute, has been elected to honorary membership in the Royal Medical Society of Edinburgh.

The twenty-first Duddell Medal of the Physical Society, London, has been awarded to Dr. F. W. Aston, fellow of Trinity College, Cambridge, in recognition of his invention and development of the mass spectrograph.

The Alfred Noble Prize of $500, awarded for an "outstanding paper in electrical engineering," was presented on January 27 at a joint meeting of the American Institute of Electrical Engineers and the Institute of Radio Engineers to W. R. Wilson, engineer with the General Electric Laboratories at Pittsfield, Mass.

The Medalla Oficial, National Order of Merit, Carlos Manuel de Cespedes, has been conferred on Dr. J. C. Geiger, director of public health of the City and County of San Francisco. The citation refers to Dr. Geiger as "a talented physician and scientist, humanitarian and loyal friend of Cuba and other Spanish American countries."

The 1944 awards of the Albert and Mary Lasker Foundation, $500 in cash with a plaque and scroll, were presented, on January 24, to Dr. John MacLeod, of the department of anatomy of the Cornell University Medical College, and to Dr. Felix J. Underwood, executive officer of the Mississippi State Board of Health, at a dinner in New York City given at the annual meeting of the Planned Parenthood Federation of America.

The Mineralogical Society of America has elected the following officers: *President,* K. K. Landes, University of Michigan; *Vice-president,* George Tunell, Geophysical Laboratory, Washington, D. C.; *Secretary,* C. S. Hurlbut, Jr., Harvard University; *Treasurer,* Earl Ingerson, Geophysical Laboratory, Washington, D. C.; *Editor,* Walter F. Hunt, University of Michigan; *Councilors,* R. E. Grim, Illinois Geological Survey, Urbana, and Michael Fleischer, U. S. Geological Survey, Washington, D. C.

Dr. Edwin B. Fred, since 1943 professor of bacteriology and dean of the College of Agriculture of the University of Wisconsin, dean of the Graduate School, has been named president of the university. He succeeds Clarence A. Dykstra, who has become the provost of the University of California at Los Angeles.

Dr. William H. Taliaferro, Eliakim Hastings Moore distinguished service professor of parasitology and dean of the Division of the Biological Sciences of the University of Chicago, has been made adviser to the president in the biological sciences. Dr. Roland W. Harrison, professor of bacteriology,

acting dean of the Division of Biological Sciences, will succeed Dr. Taliaferro as dean of the division.

DR. F. J. SICHEL, of the College of Medicine of the University of Vermont, has been promoted to a professorship of physiology and has become chairman of the department of pharmacology and physiology.

DR. GEORGE G. DEAVER, of the New York University College of Medicine, associate and medical director of the Institute for the Crippled and Disabled, and director of the program for training technicians in physical therapy, has been named clinical professor in charge of physical medicine to direct the newly established division, financed under a $250,000 grant made last spring by the Baruch Committee on Physical Medicine, to aid in the physical rehabilitation of wounded war veterans and the civilian disabled. He will supervise the physiotherapy and occupational therapy services of Bellevue Hospital and will coordinate this work with the rehabilitation opportunities afforded by the institute.

DR. S. D. RUBBO, senior lecturer in bacteriology at the University of Melbourne, has been appointed to the chair of bacteriology.

THE Eli Lilly and Company has made a grant of $2,500 to Dr. Donald Slaughter, of the Southwestern Medical Foundation, Dallas, Texas, for a study of aspergillic acid and other anti-biotics in the department of pharmacology to be carried out by Dr. A. Goth, assistant professor of pharmacology.

FRANCIS L. SCHMEHL, formerly assistant chemist in the Section of Malaria of the National Institute of Health, Bethesda, Md., has been appointed associate chemist at the Research Center at Beltsville of the Bureau of Animal Industry, U. S. Department of Agriculture.

DR. K. A. C. ELLIOTT, in charge of the Chemical Research Laboratories of the Institute of the Pennsylvania Hospital, Philadelphia, has been appointed assistant professor in neurochemistry at McGill University and a member of the research staff of the Montreal Neurological Institute.

HUGH S. BARNABY, of Purdue University, has become a member of the pharmaceutical research staff of the Calco Division of the American Cyanamid Company.

DR. H. V. HALVORSON, professor of bacteriology at the University of Idaho, has leave of absence for a year which he is spending at the University of California at Berkeley, working in the laboratory of Professor W. V. Cruess and Dr. R. H. Vaughn.

DR. WEI CHANG CHU, instructor in pharmacology at the Kweiyang Medical College, arrived in San Francisco on January 24. He has leave of absence from the Chunking Government for two years for work in the department of pharmacology of the School of Medicine of Stanford University.

THE *Journal* of the American Medical Association reports that Dr. Maurice L. Tainter, director of research, and Dr. Chester M. Suter, director of chemical research, of the Winthrop Chemical Company, Inc., Rensselaer, N. Y., and New York City, have arrived in Cairo on invitation of the Egyptian Government, to assist in research on tropical diseases. They will spend several months investigating malaria, schistosomiasis, a liver infestation and trachoma.

DR. G. M. BENNETT, professor of chemistry at King's College, London, has been appointed government chemist in succession to the late Sir John Fox, F.R.S. He will take up this work in the late summer of the present year.

DR. GERALD WENDT, science adviser of Time, Inc., will give a series of eight lectures beginning on February 9 for the John L. Elliott Institute of Human Relations. The course, entitled "Science Challenges Society," will be given on Friday evenings from February 9 to March 30.

DR. ALBERT F. BLAKESLEE, of the department of botany and the Genetics Experiment Station of Smith College, from January 18 to 25 gave lectures at the University of Arkansas, Fayetteville, at Oklahoma A. and M. College, Stillwater, and at the University of Oklahoma, Norman, on "Controlling Evolution and Life Processes in Plants." He also spoke before biological seminars at these institutions on "Gene Mutations in Datura" and gave after-dinner talks on "Our Expanding Universe of Knowledge and Adjustments Necessary in Research and Education."

AT the request of the War Committee on Conventions, Washington, D. C., the Institute of Medicine of Chicago has cancelled its Midwest Conference on Rehabilitation, which it had planned to hold at Chicago on February 12.

To cooperate fully with the government in meeting difficulties of transportation, the annual spring meeting of the American Chemical Society will not be held in 1945.

THE Cold Spring Harbor Symposium on Quantitative Biology, on "Variability and Heredity in Microbiology," which was planned for this summer, has been postponed until next year. This decision was reached by the Board of Directors of the Long Island Biological Association, at its January meeting, because of the uncertainties of travel and the difficulty of securing the necessary labor to maintain living quarters and food service.

As a result of a conference of fifty business leaders held in New York on January 12, a committee of eight industrial executives, with Charles E. Wilson, president of the General Electric Company, as chairman, has been appointed by the Secretary of Commerce to advise the department and the American Standards Association of future plans for standards work and to make recommendations in regard to the relative roles that should be played by government and industry in standards activities. Serving with Mr. Wilson on the committee are: Frederick M. Feiker, dean of engineering, George Washington University; Clarence Francis, chairman of the Board of the General Foods Corporation; Ephraim Freedman, R. H. Macy and Company, Inc.; Frank B. Jewett, president of the National Academy of Sciences; William B. Warner, president of the McCall Corporation; Arthur D. Whiteside, president of Dunn and Bradstreet, Inc., and R. E. Zimmerman, vice-president of the U. S. Steel Corporation. The conference, presided over by Wayne C. Taylor, Under Secretary of Commerce, recommended that industry should provide strong leadership in the development of national standards and that this should be done in full cooperation with the Government.

An editorial article in the Richmond *Times-Dispatch* calls attention to the program of conservation now being developed by the Virginia State Department of Education under the immediate direction of A. L. Wingo. The project was originally suggested by Dr. Wortley F. Rudd, past president of the Virginia Academy of Science and of the Southern Association of Science and Industry. It has as its ultimate aim a course of study in the public schools to acquaint Virginia children with the material potentialities of their respective communities and of the State as a whole.

At the University of California at Los Angeles, fellows working in organic chemistry are Dr. Philip H. Dirstine, holder of the Dow post-doctorate fellowship, and Tod W. Campbell, holder of the Abbott fellowship. Seymour Lindenbaum, Sharp and Dohme research assistant, is working on the synthesis of compounds related to Vitamin A. In the biochemical fields allied with the amino acid research of Dr. Max Dunn are research associates Dr. S. Shankman and Dr. H. F. Schott and research assistants, Bruce Merrifield, Merrill Camien, Louis B. Rockland, John Murray, E. A. Murphy and Willi Frankl. Among the subjects they are investigating are yeast proteins, amino acids in animal nutrition and amino acids in micro-biological analysis. Dr. William G. Young, chairman of the department, stated that grants and their donors include the U. S. Quartermaster Corps, $10,000; the Committee on Medical Research, $36,000; the Nutrition Foundation, $3,000; Gelatine Products, $5,000; Sharp and Dohme, $2,700; Dow Chemicals, $2,400; Schering-Glatz Company, $1,800; Merck and Company, $1,500; Anheuser-Busch, $1,500; Vio-Bin Corporation, $1,000; the Abbott Laboratories, $750. An additional grant of $7,500 from Swift and Company will be used when conditions permit.

A Division of Food Technology has been established at the Massachusetts Institute of Technology to study post-war problems of world food production, including the improvement of products, and methods for retaining natural flavors and nutritive elements in processed foods. Under the department of biology and biological engineering it will be directed by Professor Bernard E. Proctor, for many years a member of the staff, who has returned from leave of absence as director of subsistence and packaging research for the Quartermaster Corps of the United States Army. The program includes a new five-year course offering special opportunities for returning service men in the field of food technology. Each student will spend at least six months in food manufacturing plants. The new laboratory bears the name of Samuel Cate Prescott, who until his retirement in 1942 was for many years head of the department of public health.

It is reported that the Brewing Corporation of America, Cleveland, plans to spend $250,000 for research on the development of new food products based upon the nutritional values of spent brewers' yeast.

An anonymous gift of $100,000 has been made to the School of Medicine of Stanford University and the sum of $50,000 for use in gathering reference material for the Hoover Library.

The Nuffield Foundation has established a department of neurology at the University of Liverpool. The services of the department will be available both to voluntary and municipal hospitals throughout the district. The trust, after considering a report on the proposal by its Medical Advisory Council, has made a grant to the university of £3,000 a year for five years, and the balance of the income required is now being collected. A promise of the capital expenditure which will fall upon the university has already been obtained from an anonymous benefactor. The trust will make available financial assistance to the extent of £15,000 to enable the University of Leeds to establish a whole-time chair in psychiatry, with which will be associated a complete psychiatric unit. Facilities will be provided for both undergraduate and post-graduate instruction and for research in the various branches of psychological medicine as well as for treatment.

The correspondent at Ottawa of *The Times*, London, reports that the Commonwealth and Empire Conference on Radio for Civil Aviation has recommended the establishment of a permanent central office in London for the remainder of the war. The conference has been examining war-time radio developments such as radar and their application to civil flying. At the closing session Sir R. Watson-Watt, head of the British delegation, said that projects that have been studied at Ottawa will be further examined and tested by radio and aviation authorities in the countries of the Commonwealth during the next few months and that the data made available would finally become the subject of international consideration.

The information *Bulletin* of the Embassy of the U.S.S.R. states that five miles from Tashkent the Uzbec Scientific Research Institute of Forestry is laying out a park. On an area of about a hundred acres a protected zone has been planted with lanes of oaks and sycamores, poplars, walnut trees, chestnuts, limes, fruit trees and roses. There is a nursery containing a hundred and forty different types of trees and bushes. A meteorological station has been established to study prevailing winds. It is hoped to grow about a thousand, five hundred different kinds of trees and bushes. The park will be the largest nursery in the Republic, from which state farms, collective farms and towns will be able to obtain specimens of new types of plants.

DISCUSSION

THE MEANING OF HYDROPONICS

Correct terminology is requisite to scientific progress. The incorrect terms which were used in attempts to describe soilless crop production before its scientific basis could be clarified have caused wide misconceptions of its principles and have markedly delayed the establishment of this method to wide use.

Soilless crop production consists of growing crops in water, containing chemicals. Large shallow basins for the water, and wood shavings, sawdust, straw or other waste vegetable litter for seedbeds which support the plants in the water are essential equipment. Water causes the architecture of the roots of plants to become different from those growing in the soil. These differences in architecture are reflected in the functions of the roots. For this reason some crops can be grown more economically without soil than with soil, and by the same tokens others can not.

The revolutionary feature of soilless crop production consists in the substitution of the dynamics of fluids for the dynamics of a porous solid in the universe of growth of land plants. Fluids can not provide anchorage for the roots, hence their architectures become different from those growing in the soil. This change is according to a fundamental biologic law—an organ atrophies or changes in form and function in an environment in which some of its functions can not operate. In the differences of root growth of plants in water from those of the soil is a universe of new phenomena whose interpretation can be formulated into a distinctive category of knowledge.

Because plants grow according to the activities of their roots, and as the dynamics of water changes these from their soil types according to a pattern that can be described and formulated, hydroponics[1] meaning *water working* was chosen as the name for the art and the science of crop production without soil.

Terms as chemical farming, chemiculture, nutrient solution culture and kindred expressions not only were inappropriate but did great harm to this development in its crucial formative period, as they created a wrong perspective concerning the scientific basis of soilless crop production. These terms projected the functions of the nutrients into the foreground and thereby distorted their relative position of importance to other essential factors. This distortion obscured the perspective of the outstanding determinants of the system—the dynamics of water and the physical influences of the seedbed. Likewise, the term soilless agriculture is misapplied, as it is contradictory in meaning and implication—agriculture infers land, that is, solid matter as the home of the roots of plants.

The creation of soilless crop production depended on the solution of three scientific problems. They were:

(1) Establishment of the use of economic materials and the development of simple practical procedures in place of the costly refined materials and the complicated techniques employed in the growing of plants in small glass containers filled with nutrient solutions, in scientific laboratories for experimental studies on the mineral nutrition.

(2) The complete divestment of the water culture method of crop production from the laboratory concepts of water culture which were designed to study the mineral nutrition, in order that hydroponics be provided with its own distinctive basis—the dynamics of fluids substituted for that of porous solids on the root growth of plants. The divestment was necessary in order that the right approach to the practical use of the method could be established.

[1] W. F. Gericke, Science, 85: 177–8, 1937.

(3) The formulation of the dynamics of water. This involved, (*a*) explaining why the roots of plants when grown in nutrient solutions become different from those grown in the soil; (*b*) formulating the pattern as to how they become different; (*c*) describing how the hydroponic technique is arranged for various species in various climates to meet the requirements of a changed root system; (*d*) interpreting the significance of differences in roots in other characters in plants, and (*e*) integrating these phenomena in the evolutionary history of vegetation.

The functions of water in hydroponics are dynamic and physiologic, in agriculture they are physiologic only as the solid matter of the soil provides the dynamic functions. In soil water exists largely as a film around solid particles, hence has little or no hydrodynamic properties. Its dynamics is that of the solid matter to which it adheres. Water in the free state in hydroponics precludes or markedly restricts (*a*) anchorage for roots, (*b*) fixity of position for roots, (*c*) resistance to penetration with its induced stimulus of roots, (*d*) temperature differentials with their induced effects, (*e*) moisture saturated atmosphere affecting production of root hairs, (*f*) and other physical conditions which affect the tectonics of roots.

The mass of the nutrients required by plants is too small to be an appreciable part of the dynamics of the medium that supplies them, hence their functions are physiologic only. The non-nutritive materials create the dynamics, control the physical influences and determine physical conditions which affect the growth of vegetation. Water is the chief non-nutrient material used in hydroponics. Its dynamics is the foundation on which the art and the science of hydroponics is formulated.

W. F. GERICKE

BERKELEY, CALIF.

VITAL RESEARCH OF AGRICULTURE

EXPERIMENTAL study of plants and animals for the purpose of feeding, clothing and sheltering the human race should be called "vital research." Webster defines "vital" as "essential to the continuance of life" and "necessary to life." Thus, the word accurately describes research that will aid the producer to supply food, clothes and shelter, as well as raw materials for industrial uses. The benefits are commonplace in times of abundance, but are likely to be dramatic when there is a scarcity of the daily essentials. The responsibility of the agricultural industry to provide ample food is heavy now and will be tremendous in the postwar period.

Much agricultural investigation is of the vital type, since it attempts to solve some producer's or consumer's problem that is impairing production, quality, food value or return for the consumer's dollar. Farmers, farm advisers (county agricultural agents) and scientists at the agricultural colleges are daily pointing out and working to solve such problems. The broad objective is not only to furnish plenty, thus eliminating the specter of starvation, but also to provide the particular kinds of food that are essential for human vigor. These general characteristics apply also to studies outside the field of agriculture—for example, medical research.

It is essential for a group of research people to have a goal; a definite, simple objective is necessary to the industry served, both for training young people to solve problems and for guiding mature workers. Naturally vital research, with its broad problems, its fixed goals and often its limited time for accomplishment, demands scientists of wide training. Frequently it requires the cooperation of several workers in related fields, since the practical production of plants and animals involves wider extremes of heredity and environment than some other types of research. The investigator must keep abreast of agricultural, industrial and economic trends if he is to assist the producers in applying scientific principles intelligently to their problems.

A recent statement in the *A.A.A.S. Bulletin* is of interest in this connection: "There appear to be two principal important functions of the Association in the near future, as there have been in the recent past. One is to keep ever before scientists the fact that science as a whole is much greater and richer than any of its parts, and that extreme specialization and isolation will in time lead to sterility and decline. The other is to emphasize the obligations of scientists to society and, reciprocally, to make clear to the intelligent public how greatly society depends upon science.[1] It is hoped that these two simple goals and the results of vital research will enrich science, besides insuring the essentials of life. Considering the frequent occurrence of new problems and the ever-changing trends of agriculture, it is difficult to see how "sterility and decline" will take place in vital science if the vital-research worker keeps firmly in mind his role of service to industry.

There are numerous examples of work that will fulfil the qualifications for vital research. The use of proper environment and non-bolting strains has prevented the premature seeding of celery and other biennials; a change in plant composition has led to increased fruitfulness; yield and sometimes quality have been improved through the use of hybrid seed corn or onions; the deficiency effects of essential ele-

[1] "Democracy in Science," *A. A. A. S. Bulletin*, 3: 50–51, 1944.

ments in both plants and animals have been discovered, and the proper corrective measures applied. A quickly devised procedure for combating mites has saved many tons of tomatoes for processing; an accurate method for determining butterfat content of milk has greatly advanced the dairy industry and inaugurated new research projects; disease control has made livestock concentration possible and stabilized financial investments therein; the amount of labor required to produce crops and improve quality has been reduced through labor-saving machinery; and a more accurate knowledge of the labor requirement of various crops has provided essential data on their relative desirability for food production during periods of stress. In projects of this sort the worker has been closely in touch with the needs of the industry.

The Hatch Act of 1887, in establishing agricultural experiment stations, defines their purpose as follows: "To aid in acquiring and diffusing among the people of the United States useful and practical information on subjects connected with agriculture, and to promote scientific investigation and experiment respecting the principles and applications of agricultural science." Vital research is the purpose of this act. The early agricultural studies indicated a desire to solve vital problems affecting the food security and health of our citizens and thus to increase our agricultural wealth. This point of view predominated for some time. With the increase of staff members, there gradually developed at some stations a group primarily interested in more indirect applications or in merely widening our horizon of knowledge. The value of much of their work and training has been proved repeatedly, but most vividly when the war suddenly focused our attention on providing food, shelter and clothing. For the first time in many years, workers in other sciences were striving with agricultural personnel towards a common goal. The constructive gains made through this cooperation must be preserved. Vital research needs the cooperation of all workers.

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THE ACTION OF AMINO ACIDS ON COLOR CHANGE IN FUNDULUS

IN the course of some work on Fundulus it was noticed that those fish that were injected intraperitoneally with a mixture of amino acids turned dark in a few minutes if they were light or if they were dark and removed to a light environment they remained dark.

The fish were injected with a mixture of amino acids[1] in 15 per cent. solution containing amino acids as derived from the acid hydrolysis of casein fortified with tryptophane. The approximate analysis as furnished by the manufacturer is: Total nitrogen 2 per cent., alpha amino nitrogen, approximately 75 per cent. of total nitrogen, tryptophane 1 per cent. of amino acids, calcium 0.01 per cent. to 0.02 per cent., sulfates 0.01 per cent., phosphates, iron and magnesium a trace. pH approximately 4.0.

The fundulus were removed from the aquarium and immediately injected intraperitoneally through a 27-gauge needle with doses ranging from 0.05 cc to 1 cc of the mixture of amino acids. They were placed in containers of either aerated or running sea water, some of which were over light backgrounds and others over dark.

With doses of 0.5 cc and 1 cc none of the fish turned light and those that were light before injection turned dark in about five minutes. Controls uninjected and injected intraperitoneally with 1 cc of sea water turned light when placed over a light background. The controls injected with 1 cc sea water survived, as did those injected with 0.5 cc amino acid mixture. Those injected with 1 cc of the amino acid in the morning died during the night; their abdomens were very red and swollen.

This information is published for the benefit of those interested in color changes in fish, as the writer has no intention of pursuing this problem.

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A STRANGE COINCIDENCE OF ERRORS

IN clearing out old papers I am reminded of a most curious coincidence of errors which hitherto has never been fully published. My late colleague, F. E. Fowle, and I determined the dispersion of rock salt, as published by Langley in Volume I of the *Annals of the Smithsonian Astrophysical Observatory* in the year 1900. Our values of wave-length and refractive index were fitted by a least squares solution to the 5-constant formula of Ketteler, by the late Professor H. H. Kimball, of the Weather Bureau. I have his original manuscript before me. Kimball computed from his constants, derived entirely from our work, the indices of refraction corresponding to the wavelengths 13.96 microns and 22.3 microns, which had shortly before been observed by Rubens and Nichols, and by Rubens and Trowbridge.[1] The following are

[1] Marketed by Frederick Stearns and Company, Detroit, Mich., under the name of Parenamine. I am indebted to the manufacturers for a supply of this substance.

[1] *Ann. der Phys. u. Chemie*, Bd. 60, 1897, pp. 454 and 733.

the computed results of Kimball and observed by these authors, respectively:

Wave-length λ	Computed n_1	Observed n	$n - n_1$
13.96	1.436526	1.4373	+ 0.000774
22.3	1.339977	1.340	+ 0.000323 [sic]
		corr.	+ 0.000023

In *Annalen der Physik,* 6, 1901, pp. 624, 625, F. F. Martens states in footnotes that for the wave-length 13.96 the German authors had made a correction,[2] giving n = 1.4627. He also points out that Kimball's constants should give for this wave-length the value 1.4635, and says: "Dieser Fehler ist . . . höchst befremdend." He then goes on to quote our values of n, cutting off from them the fifth and sixth places of decimals which had been published in Volume I.

In 1901, immediately after seeing Martens' article, I checked Kimball's work. I found that all his logarithms were correct, but that in setting down the number corresponding to the final logarithm he had erroneously transposed the figures 3 and 6, so that his value as published in the *Annals* should have read $n = 1.463526$. The corrected $n - n_1 = -0.000826$.

Later, Dr. F. Paschen made a beautiful determination of the dispersion of rock salt,[3] carrying on to much longer wave-lengths than we had done. He disagrees sharply with Martens, who thought the fifth and sixth places of decimals in n in our work should be thrown away, saying that he finds it up to 2.3 microns "von bewundernswerter Präzision." Up to and including the wave-length 4.12 his values and our values of n differ only a few units in the sixth decimal place, as shown by Table 394, p. 360, Smithsonian Physical Tables, 8th Revised Edition. I wrote to Dr. Paschen expressing my gratification and telling him the nature of Kimball's error as related above. I received a very kind reply.

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Research Associate

SMITHSONIAN INSTITUTION

RECENT HIGH MORTALITY AMONG GEOLOGISTS

IN the issue of SCIENCE for December 29 Dr. Sidney D. Townley offers a criticism of my note in the issue of May 26 under the caption "Unusual Mortality among Geologists." I there drew attention to the very high mortality, sixteen fellows of the Geological Society, for the period between November 15, 1943, and April 18, 1944, slightly more than five months.

To quote Dr. Townley, "Only two of these deaths occurred in 1943, so if we stick to annual totals it is quite probable that 1943 will show nothing unusual. . . ." The figures were available to Dr. Townley, and he could have known that the death losses for the year 1943 (15) were the highest in the society's half-century of existence up to that time, with exception of the years 1934 and 1935, when they were 19.

We entered the war a few weeks only before 1942 and the society's losses by death for the three-year war period 1942 to 1944 have been 51, the greatest for any three-year period in the 56 years of its history. This figure was approached only once; in the period 1933 to 1935, when the losses were 47 (a fraction of one per cent. higher if membership increase is taken into account). The next highest loss for a three-year period was 31.

I hold no brief for my suggestion that the latest high mortality may in part be due to the war. It was offered as a suggestion only, and I have no suggestion even to offer for the high death losses of the period 1933 to 1935. Dr. Townley tries to explain the sixteen deceased fellows of November 15, 1943, to April 18, 1944, by the large number of geologists who were drawn into the profession by LeConte, Branner and Chamberlin at the time when the sixteen must have been undergoing their training. Unfortunately for this hypothesis no one of the sixteen came under the training of any one of the three, as reference to "Who's Who" would have shown.

WILLIAM H. HOBBS

SCIENTIFIC BOOKS

PHYSICS FOR THE GENERAL READER

Physics Tells Why. By OVERTON LUHR. Illustrated by Ruth C. Schmidt. ix + 318 pp. Lancaster, Pa.: The Jaques Cattell Press. 1943. $3.50.

THE modest subtitle of this book is "An Explanation of Some Common Physical Phenomena." Actually the book does more than this implies since, in addition to explaining many phenomena, it also gives a systematic development of the elementary principles of physics, grouped in nearly the usual manner under mechanics, electricity, light, heat and sound, with a concluding chapter on radiation and atomic physics. Thus the basic framework is not far from that of the traditional text-book of general physics.

There is, however, a marked difference from the usual text, aside from the omission of numerical problems and all but a few of the most elementary equations. This difference, which incidentally justifies the subtitle, is that the reader is led to basic principles, not by laboratory experiments designed to illustrate them, but by ordinary experiences of household, street and field. A certain degree of precision

[2] *Ann. der Phys. u. Chemie,* Bd. 61, 1897, p. 224.
[3] *Ann. der Phys.* Bd. 26, 1908. See pp. 120, 121, 132.

is sacrificed by this method, but a book intended for readers without special training must in any case be mainly descriptive. The loss is more than offset by the advantage of letting the reader draw on his familiar experience rather than labor to understand the reasons for details of experimental procedure.

The method of Dr. Luhr's book is one which has been tried in others, especially in some of the more recent high-school texts, not always with much success. It requires of the author the clearest perception of his subject and a very thoughtful discrimination. The natural temptation is to be timely and so draw illustrations from the recent developments of technology, about which the reader's curiosity is awake because he has not yet learned to take them for granted. These developments, just because they are the latest products of a complex technology, generally involve so many principles in combination that they often make the least suitable illustrations for the beginning reader.

In avoiding this temptation, Dr. Luhr has not only explained the elements of physics with an admirable simplicity and clarity, but he has done something even more worth while in arousing the reader's wonder about things that are in front of his eyes every day. For this reason especially, the book should be recommended to boys and girls of high-school age.

The illustrations by Ruth C. Schmidt have an agreeably offhand character, as if the manuscript had fallen into her hands by accident and she had made marginal sketches by way of commentary as she read it. The appearance is doubtless deceptive; they probably required work enough. Those which show human figures (if the word "human" can be so far extended) are sympathetic if also somewhat ironic caricatures of man, alternately baffled, determined and delighted in his quest to understand the world around him.

In reading this lively book, it is hard to realize that it was written by a man in a losing struggle with an illness which took his life before the work was printed. The manuscript was prepared for publication by Ralph Johnson. This work of friendship must have been done conscientiously, as the book is very free of such small errors as an author generally finds to correct in a last reading of his manuscript, if he does not miss them even then. One which escaped in the present work may perhaps be worth mentioning. The statement that "Aristotle, as well as most of the other learned men of Ancient Greece and Rome, believed that the earth was flat" slights the work of the early astronomers, who had not only shown that the earth is spherical but had also found how to measure its radius. But this is of negligible importance in a book which is not intended as a history and which succeeds admirably in the purpose for which it was written.

Atoms in Action. By George Russell Harrison. xii + 401 pp. Garden City Publishing Co. 1944. $1.49.

This is an inexpensive, though enlarged, edition of the work which appeared under the same title in 1937. Its subject is physics, especially applied physics, and it offers, in a lively style and intelligible form, a remarkable amount of information in this diverse and rapidly changing field. It sustains a high degree of clarity over the whole range of applied physics, including among other subjects spectroscopic analysis, radio communication and the physics of agriculture and medicine.

Since the field is contemporary and the author's intention was to be up-to-date, he had to face the difficulty, referred to in the preceding review, of explaining physics by its more complex rather than its simpler phenomena. This has been skilfully done. A certain familiarity with technical and scientific terms is assumed, but not much more than is taken for granted by writers on science in the daily papers. The reader who has had a good introductory course in physics should find no difficulty with the book. The reader with only the kind of knowledge which any one is likely to have acquired by a reasonable awareness in a technological culture will probably understand most of it, though he might do well to read, for example, "Physics Tells Why" as an introduction. A person with much more knowledge of physics will still be almost certain to learn a great deal that he did not know before.

The section which has been added in the present edition deals with physics in the war and afterward. Because the rest of the book was widely reviewed in the first edition, the part which is new naturally invites the especial attention of the present reviewer. It has besides a particular interest in that it contains an exposition of the author's view of the social consequences of science, a view which could only be inferred from occasional discursive remarks in the earlier edition. Since the jacket carries the announcement that "Atoms in Action" has the unqualified endorsement of the American Institute of Physics, many readers may assume that the social outlook of its author has some official recognition as that of American physicists generally.

This outlook may be briefly described as a materialistic optimism. In calling it materialistic, I do not mean to imply that the author is apathetic to intellectual and spiritual values, but he believes that these follow automatically fom the material gains of applied science. Scientific research is thus the key to every sort of progress, and, now that mankind has found this key, improvement—material, intellectual, and spiritual—has a mechanical inevitability. Thus he says:

Nature provides an automatic compensating mechanism, such that if material progress is too rapid, suffering results which accelerates spiritual progress.

And in another place:

Civilization contains innate self-stabilizing influences. Society has certain problems to solve and definite lessons to learn. The function of science is to speed up this learning process. If modern wars seem more terrible, it is because we are learning our lessons faster and overcoming more rapidly those obstacles to human progress which must be met in any case.

Certainly no one will doubt that scientific research provides means which may be used for human progress, but that there is any automatic mechanism to insure that these means will be so used is a debatable thesis, doubted by many thoughtful and well-informed people. It was a good while ago but already within the age of modern technology that John Stuart Mill wrote: "Hitherto it is questionable if all the mechanical inventions yet made have lightened the day's toil of any human being." Most of us would doubtless count this an exaggeration. But I think we should find it harder to dismiss the opinion of Henry George, that "the new forces [of material progress], elevating in their nature though they be, do not act upon the social fabric from underneath, as was for a long time hoped and believed, but strike it at a point intermediate between top and bottom. It is as though an immense wedge were being forced, not underneath society, but through society. Those who are above the point of separation are elevated, but those who are below are crushed down." And indeed one can not help wondering whether what the world has now would pass for civilization with Socrates, let us say, or Pascal or, for that matter, with any barefoot and illiterate South Sea Islander caught between the bombs and shellfire of the technically advanced nations.

But, in any case, it is to be hoped that "Atoms in Action" will have many new readers. They will find that nature is not niggardly of either her secrets or her riches, and the world can be made incomparably better by knowledge, employed with good-will. And if, like this reviewer, they can not share Professor Harrison's optimistic belief that this will happen automatically, they may be moved themselves to try to make it come true.

R. T. Cox

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ORGANIC SYNTHESES

Organic Syntheses. Vol. 24. An annual publication of satisfactory methods for the preparation of organic chemicals. Nathan L. Drake, editor-in-chief, with an editorial board and an advisory board. Pp. 119. New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd. 1944. $2.00.

The syntheses described in this new volume of this important series are the following: Acenaphthenequinone, Aminoacetal, 4-Amino-2,6-dimethylpyrimidine, *dl-alpha*-Amino-*alpha*-phenylpropionic acid, 4-Amino-1,2,4-triazole, Benzoyl cyanide, Benzoylformic acid, *tert.*-Butyl acetate, *o*-Chlorobromobenzene, ω-Chloroisonitrosoacetophenone, 2-Chlorolepidine, 1-Chloromethylnaphthalene, Coumarilic acid, Cyclopropanecarboxylic acid, *nor*-Desoxycholic acid, 3,12-Diacetoxy-*bisnor*-cholanyldiphenylethylene, γ-Di-*n*-butylaminopropylamine, 2,6-Dichloroaniline and 2,6-dibromoaniline, Diphenyldiazomethane, Ethyl diazoacetate, Ethyl hydrazinecarboxylate and diaminobiuret, Ethyl-N-tricarboxylate, Glyoxal bisulfite, 4(5)-Hydroxymethylimidazole hydrochloride, 4-Methylcarbostyril, 4-Methylcoumarin, Methyl pyruvate, *o*-Nitrobenzaldehyde, *p*-Nitrobenzyl acetate, *p*-Nitrobenzyl alcohol, Phenylmethylglycidic ester, 1-Phenylnaphthalene, *alpha*-Phenylpropionaldehyde, Selenophenol, Sorbic acid, Undecyl isocyanate, Vinylacetic acid.

The concluding subject index covers volumes 20–24.

In other respects the volume is exactly like its predecessors, Vol. 23 having been reviewed somewhat more fully in Science of August 27, 1943, page 200.

Marston Taylor Bogert

Columbia University

REPORTS

THE NEW YORK ZOOLOGICAL SOCIETY[1]

It is extraordinarily encouraging how the affairs of the Zoological Society progress even during the stress of this war. Public interest, together with the moral and financial support coming in from many quarters, is evidence of the importance and permanence of the things that this institution stands for and of its potentialities in the future.

Usually at these meetings it is the president's duty to report to the members as to the past year's happenings. With your permission I shall only do this most briefly and then go on to consider some plans and ideas for the future.

The Year 1944

The year 1944 again gave us confidence to believe that our services provided real contributions to public

[1] Address of Fairfield Osborn before the New York Zoological Society, January 9, 1945.

morale, recreation and education in this time of war. More than 2,100,000 people visited the Zoological Park despite the curtailment in automobile driving. Every service, exhibit and park area was fully maintained. This was due to the energetic and intelligent work of our staff together with all members of the organization. Services to public schools show a higher number of school classes serviced with films and slides than in any previous year. Research work of definite value to the war effort, as well as to pure science, was accomplished. Specific designs for the future development of the Zoological Park and for a new aquarium have been brought to the final blueprint stage, awaiting execution in those days of peace which we must continue to pray may not be long deferred. In these matters we have received the finest kind of cooperation from the commissioner of parks and from his staff.

Lastly, we ended the year in good financial order, with our expenses within our income and with reserves established which will help to meet the many demands that will fall upon us in the future.

Books and Films

Outside the immediate physical areas of our institution we have been able, together with the men of eight other scientific and educational institutions, to contribute towards the preparation of a series of books on the natural history of the Pacific. Preliminary announcement of this project was made at last year's meeting. "The Pacific World," the first of this series, was published during last summer in two editions—one for the Armed Services, the other for the general public. This first general book has already gone to several printings. It is being followed by a series of detailed books on various branches of zoology and natural history, written by men eminent in their special fields. Those of us who have had the opportunity of taking part in this enterprise are very grateful for it and believe that this Pacific World Series will prove an important contribution to zoological and natural history literature.

In passing, those of you here to-night who attended the 1942 meeting will probably recall seeing a film we had just made on bird migration. This film was made before war started, and due to the war we have not been able to work on any others. However, you will be deeply pleased, I am sure, to learn that this film has had a tremendous success—has been shown throughout the country, in Canada and Australia, as well as in South and Central America. Further, arrangements have recently been concluded for its distribution in Europe as well as in China, both through the theaters and through Government agencies. It provides a promise for what we shall look forward to accomplishing in the field of educational films when conditions again permit.

Tropical Research Department

To the long list of his many remarkable accomplishments, Dr. William Beebe is now about to add another. Because of the great interest aroused in Venezuela by the work of Dr. Beebe and his staff two years ago, that Government has turned over to the Tropical Research Department a building which will be used for laboratory purposes, situated west of Caracas in Venezuela. The establishment of this station is being substantially aided by the Standard Oil Company of New Jersey and by the Creole Petroleum Corporation (of Venezuela).

This property, known as Rancho Grande, is on a mountain-top, 3,000 feet up in the midst of the undisturbed jungle of a preserved national park. Dr. Beebe and his staff will spend six months in 1945 at this wonderful locality. Studies will include the conservation of wild life in the tropics and the habits of living creatures in the jungle. This will be the forty-fifth expedition of the department. A series of lectures will be delivered in the principal cities of Venezuela by Dr. Beebe and his staff. This project is the kind of work that will contribute, in the best possible sense, to better understanding between this country and the other republics of this hemisphere.

Zoological Park—New Projects

Now as to immediate as well as long-range future plans. On Members' Day, next June, we shall open a new information and educational service unit in the Zoo. This will be a place where serious-minded visitors, who really want to add to their knowledge of animal life, can be intelligently served. We are more and more impressed with the fact that the public comes to learn as well as to have a good time. I should add here that the plans for the new aquarium include similar elements for serving the public as richly as possible. In addition, we shall have ready for next spring's members' meeting two new exhibit units—one for otters, the other for raccoons. These are to be made free of bars or wire and in naturalistic settings.

Establishment of Department of Insects

Of much greater importance—we are going to establish this year a new department, namely, that of insect life. It is a curious fact that we as a zoological society, having dealt with mammals, birds, reptiles and aquatic life, have not heretofore had a department for the exhibition and study of insects and allied forms of life. We do not need to remind ourselves that insects are far the most numerous of all living things

on the face of this earth. In many respects they affect man's life, for example, in health and agriculture, far more directly than any other forms. This program contemplates the eventual establishment of a major building in the Zoo. Here there will be shown living insects of many varieties, native types as well as those from other parts of the world. Further, it will be our aim to build up this project to a point where it will become a center of study as well as public information regarding these fascinating, sometimes beautiful yet frequently troublesome and even harmful forms of life.

Scientific Research

Another aspect of our thinking for the future involves the widening and extension of our present work in the fields of research; more specifically, in comparative physiology, pathology, anatomy and bacteriology, together with studies in the field of animal behaviorism. To this end there has been established since our last meeting a scientific advisory council, of which we are honored to report the following have become members:

Dr. Alfred E. Emerson, Department of Zoology, Chicago University.

Dr. Alan Gregg, director of the medical sciences, Rockefeller Foundation.

Dr. K. S. Lashley, director of the Yerkes Laboratories of Primate Biology.

Dr. John S. Nicholas, Sterling professor of zoology, Yale University.

Dr. George M. Smith, Yale University School of Medicine.

Dr. A. Raymond Dochez, of our own board of trustees, of Columbia University and of the Committee on Medical Research of the Office of Scientific Research and Development.

As one of our council members expresses it, "the Zoological Park as well as The Aquarium have a unique opportunity for the study of a wide range of living animals quite beyond the scope of universities, museums or other types of research institutions." Of course, as you know, our institution has since its earliest years done a very large amount of valuable work in numerous fields of scientific research. But we can well plan to broaden our activities. We are aiming specifically at a future establishment which can be used as a headquarters, so to speak, for scientists and students from other institutions. This could well be called a "Research Center of Animal Life and Health." As another of our new council members expresses it:

As you can see, I am taking this whole situation very seriously as a possible means of enlarging the scope in our modern day Zoologist which I feel has become entirely too limited and which has produced specialists who do not have the broadness of view to see the interrelation of their own field with those others which are just as important in securing our knowledge of the animal, what it does and how it works.

Conservation

We need to face the unpleasant fact that there are two world-wide wars going on—one, man's destruction of man; the other, his destruction of the "living resources" of nature, upon which his own existence depends. What are these faint voices of foreboding? What are these whispers in the air which seem to say—"We are losing our forests"—"We are losing our soils"—"We are losing our waterways." What of it? —we say—there's plenty left. But the facts speak differently, for forest and soil and water are all interrelated and the destruction of the one element leads to the disappearance of the others. It can be said without hesitation that the velocity of destruction of these "living resources" not only in this country but in many parts of the earth is infinitely greater than is generally realized. It would be well indeed if these matters were made the subject, to a far greater degree than at present, of international collaboration. The declining land productivity of a nation can push it into war as readily as some other cause.

You will recall that the charter of our society provides that one of our major activities shall be that of work looking towards the protection of wild animal life. The history of the society in this field is a very fine one. We are trustees of the Permanent Wild Life Protection Fund, established by Dr. William T. Hornaday with the help of Madison Grant and others. Those were fighting days and among the many accomplishments in which this society can claim a leading part, were the saving of the American bison or buffalo from extinction, the prohibition of the sale of native wild game in New York State, the enactment of tariff laws forbidding the importation of wild birds' plumages for millinery purposes, the establishment of the first game act in Alaska, assistance in legislation which eventually developed into the International Migratory Bird Treaty between Great Britain, Canada and the United States. Even during the last year Jean Delacour of our staff gave valuable assistance to the United States Government looking towards the saving from extinction of the trumpeter swan, the largest of the world's wild fowl.

Now the thoughts that have come to us recently regarding our future conservation activities arise from a realization that the continuing existence of all wild animal life depends upon the maintenance of the forests, soils and streams in this country and in other parts of the world. These living resources are the basis for the preservation not only of wild animal life but of man himself. We therefore have come

to see that the society should give its active aid towards a better public understanding of what is going on. The joint project between the State of New York and our society for the post-war establishment of a conservation exhibit in the Zoological Park can well serve as a springboard for the educational services which we hope to accomplish in this most important field. At the risk of reiteration, allow me to say, in somewhat different terms, that the preservation of wild animal life not only in America but in other parts of the world depends upon preserving the habitats and living places in which animal life can be expected to survive. We hear a lot of talk these days to the effect that if our soils run out the food chemists will step in and feed us on synthetic foods and vitamins. This is a questionable possibility, and even though it could be accomplished, life would indeed be tasteless and colorless. In any case, we can not go around feeding vitamins to wild animals. Consequently, from now on this institution intends to do everything in its power to contribute to the preservation of forests and soils both here and in other countries upon which man and wild animal life alike must depend for their future existence.

SPECIAL ARTICLES

THE DEAMINATION OF "MARFANIL" AND RELATED COMPOUNDS[1]

CONSIDERABLE interest has been manifested recently both abroad[2] and in this country[3] in the use of "Marfanil" homosulfanilamide as a topical adjuvant in the treatment of gas gangrene. The general consideration of the compound (p-amino-methylbenzenesulfonamide, first synthesized by Miller, Sprague, Kissinger and McBurney[4]) as a "sulfa" drug has tended to cloud a proper consideration of its action and inactivation.

Recently we included "Marfanil" in a study of the relationship of structure to deamination of a series of substituted benzyl and phenylethylamines by amine oxidase. Because of the timeliness of the study with regard to interest in the compound, the fact that it is relatively ineffective when administered by mouth but is active when used topically, and since Evans, Fuller and Walker[2] have postulated very recently that some such mechanism plays a part in the inactivation of "Marfanil" in the body we have thought it worth while to publish a note on our results as they pertain to this compound.

The procedure was essentially that reported by Beyer.[5] The Warburg respirometer was used for the measurement of the oxygen taken up in the course of the deamination of the compounds. Guinea pig liver homogenates were the source of amine oxidase. The tests were conducted in the presence of cyanide using M/23 or M/16 concentrations of the amines before their dilution by other contents of the flasks. The compounds tested were tyramine, benzylamine, p-sulfamilphenylethylamine and "Marfanil." Each vessel

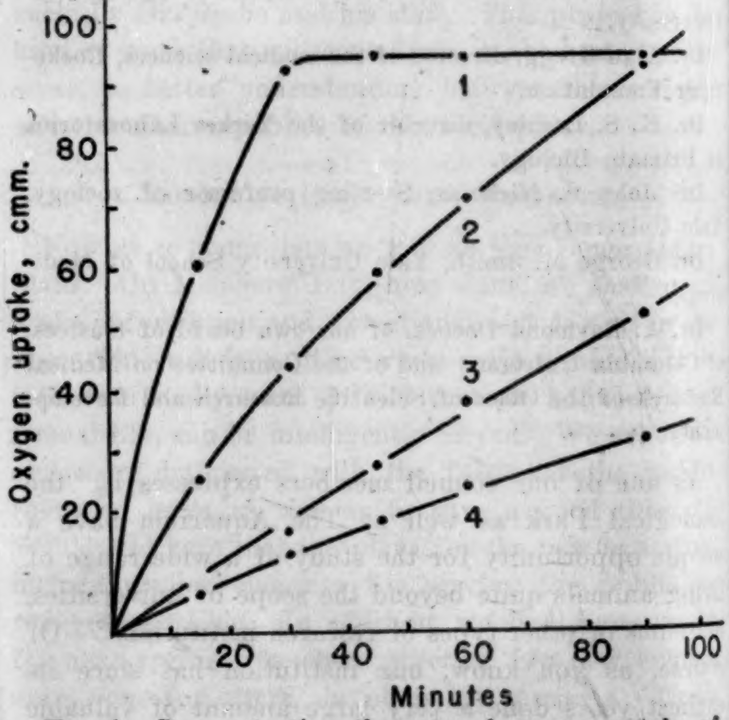

FIG. 1. Demonstrating the rate of oxygen uptake of (1) tyramine hydrochloride, M/23; (2) p-sulfamilphenylethylamine hydrochloride, M/16; (3) benzylamine hydrochloride, M/16; (4) "Marfanil" hydrochloride, M/16. 0.2 cc of each substrate was used.

contained 1.5 cc 25 per cent. guinea pig liver homogenate in M/8 phosphate buffer, pH 7.2; 0.1 cc M/15 NaCN; 0.9 cc M/4 phosphate buffer, pH 7.2. The center well contained 0.2 cc 20 per cent. KOH plus 0.1 cc M/15 NaCN. The substrates were placed in the side arms. The reaction was run at 37° C in an

[1] From the Department of Pharmacology, The Medical-Research Division, Sharp and Dohme, Inc., Glenolden, Pa.

[2] (a) J. Klarar, *Klin. Wschr.*, 20: 1250, 1941. (b) A. Fleming, Special report on tests with Marfanil prepared for Medical Research Council, 1943. (c) C. N. Robinson, *Lancet*, 2: 351, 1943. (d) G. A. G. Mitchell, W. S. Rees and C. N. Robinson, *Lancet*, 1: 627, 1944. (e) D. G. Evans, A. T. Fuller and J. Walker, *Lancet*, 2: 523, 1944. (f) G. Domagk, *Klin. Wschr.*, 21: 448, 1942; *Dtsch. Med. Wschr.*, 69: 379, 1943.

[3] (a) E. A. Bliss and H. C. Deitz, *Jour. Bacteriol.*, 47: 449, 1944. (b) C. A. Lawrence, *Jour. Bacteriol.*, 47: 452, 1944. (c) E. A. Bliss and H. C. Deitz, *Bull. Johns Hopkins Hosp.*, 75: 1, 1944. (d) C. M. McKee, D. M. Hamre and G. W. Rake, *Proc. Soc. Exp. Biol. and Med.*, 54: 211, 1943. (e) D. M. Hamre, H. A. Walker, W. B. Dunham, H. V. van Dyke and G. Rake, *Proc. Soc. Exp. Biol. and Med.*, 55: 170, 1944.

[4] E. Miller, J. M. Sprague, L. W. Kissinger and L. F. McBurney, *Jour. Am. Chem. Soc.*, 62: 2099, 1940.

[5] K. H. Beyer, *Jour. Pharmacol.*, 71: 151, 1941.

atmosphere of air. The rate of deamination of all of them was determined in the same experiment on each homogenate preparation.

The results of a representative experiment are plotted in Fig. 1. Here it is seen that tyramine is rapidly deaminated in accordance with previous findings.[5] All the compounds are oxidized, but "Marfanil" is oxidized at the slowest rate. However, the slowness with which this oxidation occurs *in vitro* is not necessarily an indication of its rate of detoxication in the body, since phenethylamine which is inactive as a pressor agent when taken orally is only slowly deaminated by this system under these conditions.

From these experiments one may conclude that "Marfanil" and certain related compounds containing an aliphatic primary amino group are oxidized under conditions wherein that action is attributed to amine oxidase. It is possible that these findings account at least in part for the usual lack of as satisfactory a systemic response to "Marfanil" when it is administered orally or parenterally as has been reported to result from its topical application.

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THE RELATIONSHIP OF LYSOZYME, BIOTIN AND AVIDIN[1]

On the basis of common source and certain similarities in chemical and biological properties, Laurence[2] has suggested that lysozyme is identical with biotin-saturated avidin. Meyer[8] found that biotin stimulates lysozyme activity when it is added to preparations containing lysozyme and avidin. Both authors have called attention to the association of avidin activity with lysozyme activity in various concentrates of avidin or lysozyme[3] and have discussed the possible identity or close relationship of these substances. A convenient method for the isolation and crystallization of lysozyme has been reported recently from this laboratory.[4] With pure lysozyme preparations available, we have investigated the relationship suggested by Laurence's and by Meyer's work.

We have been unable to obtain a stimulation of lytic activity by addition of crystalline biotin to pure or impure lysozyme preparations. In repeated trials with various lysozyme preparations and with raw egg white, biotin had no detectable effect on lytic activity as measured by the assay method of Boasson.[5] This method depends on the quantitative photometric measurement of the rate of lysis of phenol-killed *Micrococcus lysodeikticus* and is accurate to approximately 10 per cent. Numerous variables were investigated, including (1) the use of synthetic biotin (Merck) and isolated natural biotin (free acid, S.M.A. Co.); (2) ratios ranging from 10 to 1000γ of biotin per mg of lysozyme; (3) preliminary incubation at room temperature and at 37° C. of solutions of lysozyme plus biotin for periods ranging from 10 minutes to 18 hours; and (4) the use of live cells of *M. lysodeikticus*. An attempt was also made to achieve greater sensitivity by permitting both phenol-killed and live cells of *M. lysodeikticus* to lyse for 3 hours at 37°. In no case was increased lytic activity observed on the addition of biotin.

Similarly, no increase in lysis was observed when biotin was added to avidin preparations. This was true in both the presence and absence of lysozyme (Table 1, preparations 4 and 5 compared with 6). We also considered the possibility that avidin might inactivate lysozyme by combining with it and that this effect might be counteracted by the addition of biotin. However, when the lysozyme-free avidin (preparation 6) was added to an equal amount (by weight) of lysozyme (preparation 1), no repression of the lytic activity of the lysozyme took place. Subsequent addition of varying amounts of biotin to the mixture again resulted in no change in lytic activity. No evidence was obtained from any of these experiments that either avidin or biotin is involved in the lytic activity generally ascribed to lysozyme.[6]

The biotin content of our pure lysozyme is inconsistent with the hypothesis that biotin acts as a prosthetic group in lysozyme. The results of biotin assays of three lysozyme preparations, given in Table 1, are similar to those reported by Williams, Schlenk and Eppright[7] for purified proteins and enzymes (*i.e.*, trypsin, chymotrypsin, renin, insulin, casein, tobacco-mosaic virus). The purest lysozyme preparation contained only 0.009 ppm. of biotin. A 1:1 stoichiometric combination of biotin with lysozyme would re-

[1] From the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

[2] William L. Laurence, Science, 99: 392, 1944.

[3] William L. Laurence (Science, 99: 392, 1944) reported an avidin content of 100 units per gram in a six-year-old sample of lysozyme obtained from Karl Meyer (Science, 99: 391, 1944). D. W. Woolley and L. G. Longsworth (*Jour. Biol. Chem.*, 142: 285, 1942) reported that 1 mg of pure avidin is able to bind 5γ of biotin, *i.e.*, 5,000 units of biotin per gm of avidin; accordingly, Laurence's assay corresponds to about 2 per cent. of free avidin as an impurity in the sample of lysozyme.

[4] Gordon Alderton, W. H. Ward and H. L. Fevold, *Jour. Biol. Chem.*, in press.

[5] E. H. Boasson, *Jour. Immunol.*, 34: 281, 1938.

[6] After the experiments described above had been completed, we obtained 4 avidin concentrates through the courtesy of Dr. Vincent du Vigneaud. These preparations contained approximately 150, 500, 1,000 and 2,500 units of avidin activity per gram according to Dr. du Vigneaud. By E. H. Boasson's (*Jour. Immunol.*, 34: 281, 1938) method, the lysozyme contents were found to be approximately 0.5, 0.5, 0.1 and 14 per cent., respectively. The addition of biotin (270 ppm.) had no influence on the lytic activity of these preparations.

[7] R. J. Williams, F. Schlenk and M. A. Eppright, *Jour. Am. Chem. Soc.*, 66: 896, 1944.

TABLE 1

AVIDIN, BIOTIN AND LYSOZYME CONTENTS OF VARIOUS PREPARATIONS

Preparation	No.	Description	Lysozyme*	Biotin†	Avidin‡		
					Free avidin	Biotin-avidin	Total avidin
			Per cent.	γ per gm	Per cent.	Per cent.	Per cent.
Lysozyme	1	By adsorption method §; isoelectrically precipitated; crystallized once from 5 per cent. NaCl–0.2 M acetate at pH 4.5	100	0.009	0.0014	0.0002	0.0016
Lysozyme	2	By adsorption method §; not isoelectrically precipitated; crystallized twice as above and lyophilized	100	0.040	0.0036	0.0008	0.0044
Lysozyme	3	By adsorption method §; not isoelectrically precipitated; crystallized twice	100	0.12	0.0022	0.0024	0.0046
Crude Avidin Concentrate	4	By-product of lysozyme preparation by adsorption method §	16	7	2.50	0.14	2.64
Crude Avidin Concentrate	5	Preparation No. 4 further purified with ammonium sulfate as described below¶	28	38	13.2	0.76	14.0
Avidin Concentrate	6	By an unpublished adsorption method¶	< 0.1	226	82.0	4.5	86.5

* Determined by the method of Boasson (*Jour. Immunol.*, 34: 281, 1938) and expressed in terms of crystalline lysozyme prepared by the method of Alderton, Ward and Fevold (*Jour. Biol. Chem.*, in press) as the standard.

† Biotin was determined with *Saccharomyces cerevisiae* (F.B.) by the method of Snell, Eakin and Williams (*Jour. Am. Chem. Soc.*, 62: 175, 1940) as modified by Hertz (*Proc. Soc. Exp. Biol. and Med.*, 52: 15, 1943). Lysozyme was refluxed for 2 hours in 6*N* HCl to ensure complete liberation of the biotin. Added biotin was recovered quantitatively; only 10 per cent. of the added biotin was destroyed during 6 hours of hydrolysis. Biotin was freed in avidin concentrates by autoclaving at 118° C. for 1 hour at neutrality. The biotin-binding power of avidin was not always destroyed completely by the short periods of steaming at pH 4.0 in the biotin-assay method.

‡ Free avidin was measured by its biotin inactivating effect; biotin-avidin was calculated from an assay of the biotin liberated by steaming; total avidin is the sum of free avidin and biotin-avidin. Woolley and Longsworth's (*Jour. Biol. Chem.*, 142: 285, 1942) factor of 5γ of biotin per mg of avidin for the biotin-binding capacity of free avidin was used to calculate units of avidin activity to a percentage basis.

§ Gordon Alderton, W. H. Ward, H. L. Fevold, *Jour. Biol. Chem.* In press.

¶ This avidin concentrate was prepared from raw egg white by adsorption on bentonite, followed by washing with dilute potassium chloride solution and elution with alkaline phosphate buffer. The crude concentrate obtained in this way was dialyzed and further purified (after concentration by lyophilization) by solution in 2*M* ammonium sulfate and precipitation by 3.6*M* ammonium sulfate as suggested by Woolley and Longsworth (*Jour. Biol. Chem.*, 142: 285, 1942).

quire a biotin content of about 1 per cent., *i.e.*, about 10^6 times the amount actually present in the purest lysozyme preparation. Like biotin, avidin was found to be present in the lysozyme preparations only in very small amounts. All three lysozyme preparations had equal lytic activity.

A factor that may or may not have been different in our experiments, as compared with those of Meyer,[8] was the biotin content of the test organisms, and the biotin thus introduced in the assay method. Our *M. lysodeikticus* organisms contained about 0.93γ of biotin per gram of dried cells.[9] The amount of biotin introduced by the organisms would therefore be small. If, however, lytic activity involves avidin and biotin, some lysis would result when the test organism is added to avidin; such lysis did not result with our purest avidin preparation. Lysozyme was the only pure substance that lysed the test organisms.

The presence of both lysozyme and avidin in relatively impure concentrates would not be unexpected, in view of the basic nature of both of these proteins. The isoelectric point for lysozyme is about pH 10.8,[4] and that for avidin is about pH 10.0.[10] The hypothesis that the two are not necessarily related, either in biological activity or in chemical identity, is supported by several facts. Woolley and Longsworth[10] obtained highly purified avidin, which they found to be without lysozyme activity. By a different method we also have obtained avidin preparations that are essentially free of lysozyme. On the other hand, lysozyme prepared by the method of Alderton, Ward and Fevold[4] is essentially free of avidin.[11] The molecular weights, electrophoretic mobilities and solubilities of the two pure substances effectively argue against their identity. The facts presented in this paper offer no support to the hypothesis that they are related in biological activity.

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[8] Karl Meyer, SCIENCE, 99: 391, 1944.

[9] In these assays the biotin was freed for the microbiological assay (see footnote †, Table 1) by being refluxed in 4N HCl for 2 hours on an oil bath; less than 5 per cent. of the biotin present was liberated by steaming at pH 4.0.

[10] D. W. Woolley and L. G. Longsworth, *Jour. Biol. Chem.*, 142: 285, 1942.

[11] Avidin assays were made directly on the lysozyme preparations, since at pH 4 in the presence of sufficient biotin even 0.1 per cent. of lysozyme was not inhibitory to *Saccharomyces cerevisiae*. Confirmatory evidence of the low avidin content of these lysozyme preparations was obtained from balance studies on the distribution of avidin, biotin and lysozyme. Lysozyme represents about 3 per cent. of the raw egg white proteins (Gordon Alderton, W. H. Ward and H. L. Fevold, *Jour. Biol. Chem.*, in press); avidin, only about 0.06 per cent. Further experimental observations on the disposition of avidin during the isolation of lysozyme led to an upper limit of 0.2 per cent. avidin impurity in our lysozyme preparations.

THE HEART RATE OF SMALL BIRDS[1]

Ever since Buchanan[2] in 1910 recorded the heart beat of the canary as 1,000 per minute it has been known that the heart rate of small birds is very rapid. However, the quoting of these fast rates in text-books and elsewhere has created a misleading impression regarding the rapidity of bird's hearts, especially when attempts have been made to compare these early recordings with basal rates of man and laboratory animals. The heart rate of the canary as well as other small species may reach 1,000 beats per minute or even greater, but only for short intervals under conditions of excitement or vigorous exercise; basal rates are far below this figure.

In making a special study of the heart rate of small birds and mammals by means of the cardio-vibrometer, I have been particularly interested in using the heart rate as an index to the physiological response of the intact animal to environmental changes.[3,4,5,6] Because the heart rate is variable and such a sensitive "physiology-of-the-whole" indicator, it is necessary (1) to determine a basal rate or some sort of standard rate to serve as a basis for comparisons and (2) to obtain quantitative data, that is, a large number of readings over sufficient time period to obtain a true measure of heart activity. To obtain a basal rate, muscular activity, food intake, temperature and cerebral activity (fear, excitement, etc.) must be controlled since, generally speaking, these have the most marked effects on the heart rate. Removal of the unpredictable effects of the conscious centers has been one of the chief difficulties in dealing with the heart rate in the past, but with the cardio-vibrometer this factor can be satisfactorily controlled even in wild species since the heart beat together with breathing and other movements is picked up indirectly, amplified and recorded by a piezo-electric system. There are no electrodes attached to the bird, it perches normally of its own volition, and need not be disturbed in any way during the experimental period. The use of a crystal driven pen recorder facilitates obtaining a large number of accurate readings over long periods, although there is still much to be desired from the quantitative aspect.

Disregarding for the moment age, sex and seasonal variations, the average basal heart rates in round numbers of several species of common wild birds and the canary are listed in Table 1, together with the maximum rates which I have recorded immediately after flying, vigorous exercise or excitement. The basal rates represent the average rates of the birds when at rest, in a post-absorbtive but not starved condition (3–7 hours after last feeding for passerines, longer for larger birds or those with crops), in darkness, away from human presence, and at an air temperature at or slightly below thermal neutrality (about 30–32° C. for small birds). The same standardized procedure[4,5] was followed in all cases, and most of the records were made in the early evening, during the normal roosting time.

TABLE 1

Average Basal Heart Rate (Times Per Minute) in Round Numbers and the Maximum Heart Rate So Far Recorded for Small Wild Species and the Canary (Preliminary Data)

	Number of individuals	Approx. wt. (gms)	Basal rate	Maximum rate
Mourning Dove (*Zenaidura macroura*)	5	130	135	570
Towhee (*Pipilo erythrophthalmus*)	4	40	445	810
Cardinal (*Richmondena cardinalis*)	3	40	375	800
English Sparrow (*Passer domesticus*)	7	28	350	902
Song Sparrow (*Melospiza melodia*)	5	20	450	1,020
Canary (*Serinus canarius*)	10	16	514	1,000+?
Black-capped Chickadee (*Penthestes atricapillus*)	14	12	480	1,000
Chipping Sparrow (*Spizella passerina*)	2	12	440	1,060
House Wren (*Troglodytes aedon*)	4	11	450	950
Ruby-throated Hummingbird (*Archilochus colubris*)	2	4	615	?

Determination of the limits of normal heart function is, of course, only the beginning of an understanding of the heart rate. Some of the general features of the heart rate in small birds, as brought out in the studies so far, may be summarized as follows:

(1) As is to be expected, the smaller the species the more rapid the rate, but the correlation is not necessarily absolute (as can be seen from Table 1), since factors other than body size may influence a species basic heart rate. Thus, the canary appears to have a higher basal rate than wild finches of comparable size; this may be due partially to the fact that the canary has a smaller heart and lower concentration of hemoglobin in its blood than its wild relatives.[7] Likewise, the heart rate of the mourning

[1] Studies with the cardio-vibrometer aided by grants from the American Association for the Advancement of Science and the University Center in Georgia.

[2] Florence Buchanan, *Ann. Rept. Smithsonian Inst.*, 1910: 487–505.

[3] E. P. Odum and S. C. Kendeigh, *Ecology*, 21: 105–106, 1940.

[4] E. P. Odum, *Ecol. Mong.*, 11: 299–326, 1941.

[5] E. P. Odum, *Wilson Bulletin*, 55: 178–191, 1943.

[6] E. P. Odum, *Amer. Jour. Physiol.*, 136: 618–622, 1942.

[7] For canary heart size, see Buchanan, *Ann. Rept. Smithsonian Inst.*, 1910: 487–505; for hemoglobin data,

dove is apparently lower than that of the domestic fowl,[8] a much larger bird.

(2) Not enough data have yet accumulated to justify a general statement regarding the effect of sex on the heart rate in birds. In some species, such as the domestic fowl,[8] there appears to be a distinct difference between the sexes; in many other species little or no difference is evident from data so far accumulated.

(3) In wild birds, a seasonal difference in basal heart rate has been demonstrated for at least one species, the black-capped chickadee, the basal rate being 89 ± 25.1 per minute higher in summer than in winter.[5]

(4) The relation of age to basal heart rate is complicated; much depends on the air temperature being considered and the status of the temperature regulatory mechanism. In altricial species which are hatched completely cold-blooded, the heart rate at hatching varies directly with air temperature as in a frog, then gradually becomes inversely related to the temperature as temperature regulation becomes established. Interestingly enough, at a thermal neutral temperature the heart rate of nestlings of all ages, juveniles and adults of the house wren is about the same, 450/min. At 21° C. (70° F.), however, the heart rate rises from 150/min. at hatching to 600/min. at 9 days of age (when heat loss control is poor) and drops to about 490/min. in the adult[4]—reflecting in a dramatic way the ontogenetic recapitulation of poikilothermism to homeothermism.

(5) There are two types of inherent variations in the heart rate of birds as follows: (a) The rate usually decreases slightly at the peak of lung and air sac inflation and increases between breathing cycles. In mammals this relation of breathing to heart rate is apparently the reverse.[9] (b) Slower, more or less rhythmic but not regular cycles of slow and fast rate which I have called "oscillatory variations" can usually be detected. These cycles occur about 2 to 15 times per minute and the degree of oscillation varies considerably with the individual sometimes amounting to 10 per cent. of average rate for a minute period. Similar variations, presumedly related to vagal periodicity, are known in man.

(6) Any factor which abnormally lowers the heart rate below basal level tends to produce sinus arrhythmia, which also occurs in some individuals at basal level. When the heart speeds up in these individuals, arrhythmia disappears.

see Young, *Jour. Parasit.*, 23: 424–484, 1937, and Nice, Nice and Kraft, *Wilson Bulletin*, 47: 120–124, 1935.

[8] E. P. Boas and Walter Landauer, *Amer. Jour. Med. Sci.*, 185: 654–664, 1933.

[9] G. V. Anrep, W. Pascual and R. Rössler, *Proc. Royal Soc. London*, 119(B): 191–230, 1936.

(7) Heart rate-air temperature curves are very similar to CO_2 production-air temperature curves,[4] indicating that heart rate is a rough index to the rate of metabolism at least as far as temperature effects are concerned.

(8) At lower temperatures breathing rate is usually directly correlated with heart rate, but at high temperatures the relation may become inverse as a result of reflexive acceleration of breathing rate coming before a rise in body temperature accelerates the heart, since increased ventilation is a principal means of heat loss in birds.

(9) The ratio of breathing rate to heart rate appears to be significantly different in small birds and mammals, being greater than 1 to 6 in birds and less in mammals. In general, small birds breathe less rapidly but have a somewhat higher heart rate than small mammals of the same size, although comparable data are as yet few.

(10) By placing the pick-up crystal under the nest it has been possible to record the heart beat of an entirely wild bird during normal incubation in the field. During a 24-hour recording period the heart rate in the house wren ranged from 950 when the bird had just returned to the nest after a period of active flying and feeding, to 550 after the bird had remained quiet on the nest. A rate as low as the 450/min. basal recorded under controlled conditions was not recorded in the field. Also, strangely enough, the heart rate was actually higher at night than when the bird was resting quietly in daytime. This was apparently to be explained by the fact that the temperature was 20° lower at night. To get a rate as low as 450/min. under natural conditions apparently the night temperatures would have to approach thermal neutrality; during the day activity, feeding, etc., would keep heart rate above basal regardless of temperature.

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APPLYING COLCHICINE TO PLANTS BY THE AEROSOL METHOD

BOTH the published work[1] and experience of the authors indicate that a fairly sharp distinction exists between the response to colchicine application by mature meristems such as occur in trees, shrubs or herbaceous plants and the response of juvenile meristems such as the plumule. While the results with germinating seeds or very young seedlings on the whole have been satisfactory, results with more mature plants have been meager. For example, complete immersion of very young seedlings of certain species

[1] H. Dermen, *Bot. Rev.*, 6: 599–639, No. 11, 1940.

in 0.1 per cent. aqueous solution of colchicine for 4 hours has usually yielded 50 per cent. or more of tetraploids, whereas treatment of the apical meristems of half-grown plants of the same species has usually yielded none or a very small percentage of tetraploids. Since many of the most important horticultural plants are clonal varieties which can not be reproduced from seed and present only the mature type of meristem for treatment, it is desirable that a method be devised that will yield better results with this type of meristem. The striking results recently reported by Hamner, Schomer and Goodhue[2] in applying growth-regulating substances to plants by means of the aerosol method and the efficacy of the aerosol method in dispersing certain insecticides as shown by Goodhue[3] suggested that this technique might be useful in applying colchicine to plants. This report gives the results of applying colchicine in aerosol form to small seedling plants of stock (*Matthiola incana,* R. Br.) to induce polyploidy.

Approximately one hundred seedlings in the cotyledon stage in an 8-inch pan were placed under a bell jar made from a 5-gallon bottle which was sealed to a small table top by means of calking compound. In a small steel cylinder were placed one-half gram of colchicine dissolved in four and one-half grams of cyclohexanone to which was added under pressure 95 grams of methyl chloride (boiling point −23.7° C. at one atmosphere), thus making a "colchicine bomb." The "colchicine bomb" was provided with a nozzle consisting of a 10-inch length of capillary copper tubing (.014 inch inside diameter) which was introduced into the bell jar from below through a rubber stopper in the table top. When the valve was opened the colchicine "smoke" or aerosol was directed upward in the bell jar chamber and it settled on all exposed surfaces. The entire operation was carried out under a chemical hood to avoid the danger of breathing the colchicine-laden aerosol. Polyploid plants were detected principally by pollen examination but some were determined by inspection.

The range of dosage and the number and types of polyploids obtained are indicated by the data in Table 1. The total number of plants examined was 685, and 27 or 3.9 per cent. of these were pure tetraploids. Plants that were polyploid in part or all of the inflorescence totaled 136, or 19.8 per cent. of the total that survived the treatments. The greatest proportion of polyploids was obtained among survivors of treatments in which more than three fourths of the plants were killed. For example, in treatment 9, Table 1, five affected plants were obtained out of 11 survivors, or 45 per cent., and 89 seedlings were killed.

Table 1

Frequency and Types* of Polyploids in Ten Populations of Stock, *Matthiola incana* R. Br., Plants, Each Treated at the Seedling Stage with Different Dosages and Exposures of Colchicine Aerosol

Grams of 0.5 per cent. colchicine solution used	Number of plants treated†	Number of plants killed	Number of affected plants	4n	4n internal	mixoploid‡	4n epidermal	"blind"§	Percentage affected plants among those surviving
4.7	93	0	1	0	0	1	0	0	1.1
4.8	96	0	5	1	1	3	0	0	5.2
5.8	96	0	28	7	1	9	3	8	29.2
6.7	91	0	16	1	0	14	1	0	17.6
7.0	90	0	24	5	5	10	3	1	26.7
7.6	96	20	28	4	3	16	4	1	36.8
8.6	92	0	15	4	1	8	2	0	16.3
9.2	100	81	8	2	0	2	4	0	42.1
12.7	100	89	5	2	0	2	1	0	45.4
15.9	100	79	6	1	0	2	3	0	28.6

* Based on examination of the inflorescence.
† Imperfect germination accounts for populations having less than one hundred plants.
‡ Includes all other types of sectorial chimeras.
§ Plants with arrested meristems. Presumably too strongly affected for subsequent growth.

That particle size may be important in effecting penetration of the drug is indicated by the fact that several treatments in which a 2 per cent. colchicine solution was used gave a much smaller proportion of polyploids than was obtained in the main experiment. Particle size in the aerosol produced by the 2 per cent. solution is approximately twice as large as that produced by the 0.5-per cent. solution used in the main experiment.

The results of applying colchicine by the aerosol method as used were not outstanding as compared with those formerly obtained by other methods. Likewise, the aerosol method characteristically produced a high proportion of mixoploids, many of which would

[2] C. L. Hamner, H. A. Schomer and L. D. Goodhue, Science, 99: 85, 2561, 1944.

[3] L. D. Goodhue, *Ind. and Eng. Chem.*, 34: 1456–1459, 1942.

not lead to the establishment of a tetraploid race, whereas the immersion method produced only a minor proportion of such indivduals. The chief feature of the aerosol method for applying colchicine to plants appears to be that the drug may be dissolved in toxic penetrating agents of various kinds and spread on plant surfaces in sublethal amounts in a highly dispersed form, a result that could be attained in no other way. It is possible that a penetrating agent may be found that will carry colchicine into tree buds and other complicated meristems of plants when applied in aerosol form, and further work is in progress with this objective.

It should be pointed out that this method of applying colchicine to plants should not be used except under carefully regulated conditions because of the danger of breathing the poisonous aerosol.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE DETECTION OF SPERM IN THE EGGS OF INSECTS

It is frequently desirable in genetic studies to know whether all eggs laid by impregnated females have been inseminated. The usual method of preparing sections for this purpose is entirely unsatisfactory, for besides the great amount of labor involved in making such preparations, many eggs are injured or entirely destroyed in the process. What is needed is a rapid method which permits the accumulation of accurate, quantitative data that will be statistically significant.

In connection with our studies in the genetics of Drosophila, we have developed such a method which should be equally useful in similar studies on other insects. The method is as follows: Three or four eggs, which have been removed from the culture by means of a needle with a spatula-like tip, are placed on a clean slide at a distance of about one third its width from the anterior margin and arranged, properly spaced, in a row with their micropile ends all directed away from the observer. A cover-slip is then rested on the eggs and one or two drops of a physiological salt solution placed at the edge of the cover glass. Capillary attraction pulls the cover-slip down and forces the contents of each egg out through a rupture at or near the micropile. This gives a uniformly thin smear, which is more or less circular in outline.

By means of a mechanical stage, such preparations can be very quickly searched under a high-dry objective, and if sperm are present, they are easily detected. Inseminated eggs of Drosophila usually contain two or more sperm, but even though only a single sperm is present, it can be observed readily. The detection of spermatozoa in the egg of Drosophila is facilitated by the fact that they become coiled into ring-like configurations, apparently soon after entering the egg. In general, it is best to examine freshly laid eggs, although it is possible to detect the sperm as late as eighteen hours after they have been laid.

We have found this technique useful as a means for clearing up various points in genetics. It has been especially useful as an analytical method in determining zygotic viability. In certain interspecific crosses it has been possible to show by this method that secretions of the female reproductive ducts inactivate or kill the foreign sperm within twenty-four hours after mating has occurred. It is also a simple method for determining whether mating has been successful, without having to destroy the female in order to see if her sperm receptacles contain spermatozoa.

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DESTRUCTION OF FOAM IN VOLUMETRIC FLASKS

In the preparation of samples for vitamin assay we have been much troubled by foaming. Under circumstances in which we did not want to add a surface active substance, this greatly delayed accurate dilution in volumetric flasks. We have found that the foam can be quickly broken by alternate suction and its quick release.

An appropriate size of single-hole stopper is attached to a short length of glass tubing. This is thrust into a rubber hose connected with an ordinary water pump. When the foam begins to rise in the neck of the volumetric, the stopper is quickly withdrawn. The inrush of air destroys the foam bubbles.

Care must be taken not to draw off some of the foam, but one soon learns to judge the correct amount of suction to apply. The solution should also come well up into the neck of the flask to minimize the danger of implosion.

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SCIENCE NEWS

Science Service, Washington, D. C.

THE CANADIAN NATIONAL RESEARCH COUNCIL

THE Canadian National Research Council, Ottawa, has issued a review of its work during the past year, in which its important war functions in the field of science are covered. The council conducts eleven research laboratories, acts as adviser to the various government departments, and organizes and coordinates wartime scientific, engineering and technological research activities in universities, colleges and industrial laboratories throughout the nation.

This third function is performed generally through fifty "Associate Research Committees, a distinctly Canadian mechanism of proved effectiveness." These committees are set up and convened by the National Research Council, but operate as associations of the leading experts in their particular research fields. They receive financial grants, lay out programs and allocate problems to various laboratories.

This Canadian Council, set up over twenty-five years ago, has greatly expanded during the war and now directs practically all its efforts to war work. Its principal activities are in problems concerned with aeronautics, explosives, ballistics, medicine, foods, and in secret matters in which experts of the departments of national defense, munitions and supplies are collectively engaged. In addition to research problems in its own laboratories, it is supporting one hundred and sixty-two projects in the laboratories of twenty-nine widely distributed institutions.

To help it to keep informed on development by other agencies, the president of the National Research Council is a member of such service organizations as the Army Technical Development Board, the Wartime Technical and Scientific Development Committee, the Test and Development Establishment, the Canadian Inventions Board and other governmental science and engineering groups. It has an officer in London with the High Commissioner's Office. He has access to all scientific developments in England. It has a somewhat similar representative in Washington, D. C., and it has sent many scientists to the United States, England, Russia, China and Australia for liaison and contact work.

The range of studies covered by the research work of the council is wide, extending from foods and fuels to medicine and health problems and to aircraft, ships and munitions. It employs chemists, physicists, biologists, physicians, agriculturists and engineers.

Prior to the war, the primary work of the National Research Council was to foster, stimulate and coordinate scientific and industrial research in Canada. It provided scholarships for research workers in an effort to build up a body of scientifically trained young men in Canada who would remain in the country and devote themselves to science and research. The council also made financial grants to university professors to aid in research.

ITEMS

THE hundredth anniversary of Kiev Observatory can now be celebrated in the restored university buildings. The work of rebuilding the observatory—built in 1845, and thus one of the Ukraine's oldest scientific institutions—is completed. When the astronomers returned to Kiev from Sverdlovsk, a town about 1,900 miles away where the valuable equipment had been sent for safe keeping, they found the observatory building empty, its contents having been plundered by the German occupants. The older scientific men aided the technical staff in repairing the buildings and erecting the instruments, so that now regular observations are being carried out and students are again being taught in the observatory. Plans have been made to extend the observatory in the near future. Work has already begun for mounting a big modern refracting telescope. A deep basement will be built for seismic apparatus and a building will be constructed for an astrophysical laboratory.

EGGS—best replacement for point-scarce meats—may be kept in good edible condition for as much as a year by means of a new flash heat treatment developed by Professor Alexis L. Romanoff, of Cornell University. The treatment is very simple, and requires only such equipment as may be found in an average kitchen. It consists merely of plunging the eggs in boiling water for five seconds, letting them cool, and putting them away in a refrigerator. Eggs thus treated may even be kept without refrigeration, but they will stay good for only about three months, as contrasted with twelve months in the refrigerator. Cold-storage eggs remain in edible condition for about six months.

THE redder the apples the better they sell. But the right shade of green in the apple-tree's leaves is an indicator of how red the apples will be, since healthy dark-green in leaves and lively red in apple skins both result, in part, from proper adjustment in the amount of nitrogen fertilizer fed to the tree. Working on this principle, O. C. Compton and Professor Damon Boynton, of Cornell University, made careful laboratory studies of the color of leaves collected in midsummer from trees under different nutritional conditions. Using their spectrophotometer data a New York City research corporation made up a set of seven carefully compounded printing inks, with which a chart of seven leaf-green shades has been prepared. Now all an apple-grower needs to do is hold the chart alongside sample leaves from his trees, and he will get an idea of how things stand with their nitrogen nutrition. In general, high nitrogen produces apples of large size but poor color; and since color is the deciding sales factor a compromise must be sought between color and size. The work has thus far been confined to one apple variety, the McIntosh. However, since about half the apples raised in New York are of this variety, their studies are considered of particular importance for this state.